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MULTIPLE-BALLOON KYMOGRAPHIC RECORDING OF THE COMPARATIVE ACTION OF ORAL ADMINISTRATION OF ATROPINE, TINCTURE OF BELLADONNA AND PLACEBOS ON THE MOTILITY OF THE UPPER SMALL INTESTINE IN MAN*

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BOSTON

THERE is ample evidence in the literature that the belladonna alkaloids exert an antispasmodic effect on the motor activity of the gastrointestinal tract. It has been found that intestinal contractions decreased nearly 30 per cent after the administration of placebos.[1] We have therefore attempted to determine how two of the commonly used belladonna alkaloids, atropine given orally and tincture of belladonna, compared in their action with the results of the placebo studies. The time of onset of action and the magnitude of the effect of these two drugs have been noted, as has, so far as possible, the duration of their action. The results of the placebo and belladonna alkaloid studies have served as control observations with which to assess more adequately some of the recently employed antispasmodic agents.[2]

Only brief mention of the chemistry and pharmacologic action of the belladonna alkaloids is made. The important constituents of the naturally occurring belladonna alkaloids are atropine, scopolamine and levohyoscyamine. Tincture of belladonna contains 0.03 per cent of these alkaloids in about the following proportions: 90 per cent levohyoscyamine, 8 per cent atropine and 2 per cent scopolamine. Atropine consists of equal parts of levorotatory and dextrorotatory hyoscyamine, its potency being due chiefly to its levohyoscyamine content. Scopolamine is similar to atropine except that the former contains an oxygen linkage between the carbon atoms, numbers 6 and 7, on the tropine radical.[3, 4] The belladonna alkaloids act as an inhibitor of cholinergic activity. The mechanism of their action is apparently to prevent the transfer of physiologically produced acetylcholine across the effector-cell membrane. The liberation of acetylcholine at the nerve endings is not prevented, nor is the action of acetylcholine already present within the effector cell antagonized.[4]

Animal studies have shown that in general atropine weakens contractions and diminishes "tone" of the stomach, small intestine and colon.[5-7] The action of the belladonna alkaloids on the motor activity of the intestinal tract in man has been studied by various workers. There is almost complete agreement that atropine and tincture of belladonna decrease contractions, but there is disagreement concerning the effects on "tone."[8-12] Elsom et al.[8] found in man that after the hypodermic injection of 0.6 to 0.4 mg. of atropine peristaltic contractions, though often more pronounced at first, were decreased, that small rhythmical waves diminished in size though usually not in frequency and that "tone" was diminished. The effect of atropine given orally was slower, less marked and less prolonged than when it was given parenterally. Huidobro, Montero and Cuevas[9] reported a slight decrease in intestinal "tone" with 1.0 mg. of atropine given subcutaneously. According to Posey and his associates,[10] atropine given orally in doses varying from 0.65 to 1.3 mg. had no effect on "tone." These authors observed no qualitative difference in the action of atropine on the various portions of the small and large intestine, although Elsom was of the opinion that the effects of atropine were perhaps more marked on the duodenum than on the jejunum and ileum. Except for the observations of Adler et al.[11] these reports have contained little quantitative information concerning the magnitude of changes in motility produced by these drugs.

Our observations were all made in the duodenum and upper jejunum, the usual therapeutic doses of the drugs being employed. The dosage of tincture of belladonna was 0.4 cc. or 20 drops. Atropine was always given orally in dosages varying from 0.45 to 0.6 mg. The subjects were all healthy adults between nineteen and thirty-six years of age. All except 2 were males. Nine observations were made with tincture of belladonna, and 5 with atropine,

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all the tests being carried out in different subjects. Of the 14 observations with placebos, all except 2 tests were in different subjects. Eight of these subjects were included in the drug tests. The results of the placebo studies will be reported in detail elsewhere.[1] The effects of the various agents were noted on propulsive contractions, total contractions and "tone" or sustained tension of the bowel wall. Before the start of the experiments the was not started until at least 2 balloons had reached the small intestine. Four tests were run with 2 balloons, and 10 tests with 3 balloons in the duodenum and upper jejunum. At thirty to a hundred and ten minutes (average time, fifty-four minutes) after the start of the recording the subjects were given either atropine or tincture of belladonna. The effects of the drugs were followed for forty-five to three hundred and ten minutes,

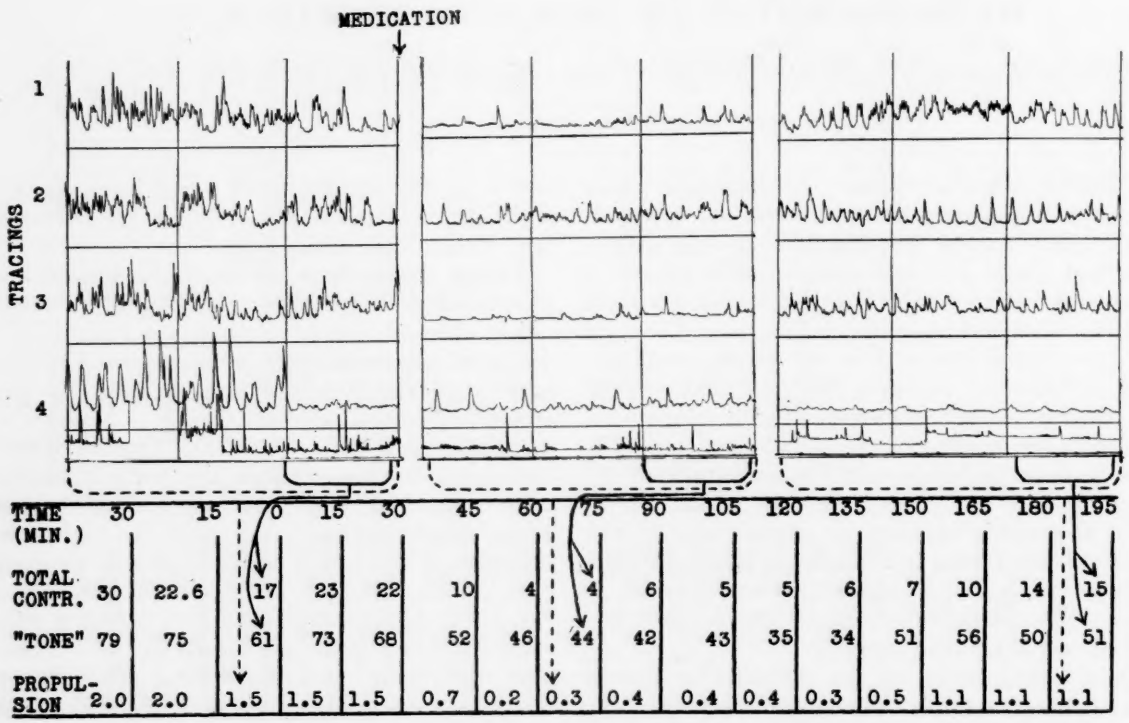

FIGURE 1. *Numerical Values Indicating Levels of Total Contractions, "Tone" and Propulsion for Each Fifteen-Minute Period before and after the Oral Administration of 0.4 cc. of Tincture of Belladonna, Together with Three Sections of Fifteen-Minute Graphic Recordings.*

The No. 1 tracing is from the upper jejunum, the No. 2 tracing from the upper jejunum or distal duodenum, and the No. 3 tracing from the duodenum. The No. 4 or stomach tracing was not used in the calculation. The vertical lines indicate time at five-minute intervals. The level of total contractions (propulsive and nonpropulsive) and "tone" were measured for five minutes previous to each fifteen-minute period and were expressed in square centimeters of surface area of the tracings. Propulsion values represent the average level per fifteen-minute period and were expressed in arbitrary units. The figure shows that forty-four minutes after the administration of the drug, total and propulsive contractions and "tone" became strikingly diminished. Beginning about a hundred and twenty minutes later intestinal motility recovered partially but remained below the control level for the remainder of the observation period shown in the graphic record. As indicated by the arrows, the sections of graphic recordings are for the following periods: fifteen minutes just prior to drug administration and intervals of sixty to seventy-five minutes and a hundred and eighty to a hundred and ninety-five minutes after administration of the drug.

subjects were informed only that we were interested in the action of various drugs on the intestinal tract. At no time were they told which medication was being administered.

METHOD

The multiple-balloon kymographic recording and the evaluation of the records have already been described.[13] The subjects reported without breakfast to the laboratory shortly after 8 a.m. and remained fasting until the completion of the tests in the afternoon. Recording of intestinal activity the average time being two hundred and ten minutes. Changes in the levels of propulsive contractions were assessed by visual inspection, the amplitude and frequency of these contractions being taken into account. Total contractions and "tone" or the sustained tension of the bowel wall were determined by measurements of the surface areas beneath the tracings at five-minute intervals previous to each fifteen-minute period. Respirations were recorded continuously with a pneumatic cuff attached around the chest. Blood pressures and pulse rates were taken for five minutes before and

at intervals of five to ten minutes for an hour after the agents were given. Symptoms were elicited by a neutral-question technic. The method used in the placebo tests was similar in all respects to the one employed in this study, except that one placebo experiment was run with only one balloon in the intestine.

Results

A graphic record, illustrating the effect of tincture of belladonna on the motility of the duodenum and upper jejunum is shown in Figure 1. After a forty-minute control period this subject was given 0.4 cc. or 20 drops of the drug. Forty-four minutes later propulsive waves and total contractions were almost completely abolished, and "tone" was decreased. For the next two hours the contractions and "tone" remained essentially unchanged. Thereafter, there was a moderate increase in "tone" and in contractile activity, which did not return to the

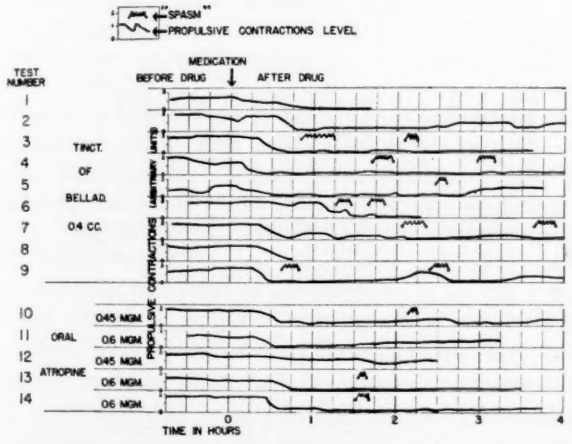

FIGURE 2. *Individual Graphs, Showing Action of Tincture of Belladonna and Atropine Given by Mouth on Levels of Propulsive Contractions.*

It can be seen that both drugs, when used in the usual therapeutic doses, caused a striking decrease in propulsive contractions from twenty-five to forty-five minutes after their administration. The exceptions were tests 6 and 12. In almost all the studies the reduction in propulsive contractions was sustained throughout most of the observation period.

premedication levels at the end of the two-hundred-and-sixty-minute observation period of the drug effect. As indicated by the propulsive contraction and total contraction values in Figure 1, there was a close correlation between the assessments of the graphic record by visual inspection and the more objective evaluation of the tracings by measurement of the surface areas representing total contractions. "Tone" was reduced at the forty-five-minute post-drug interval. For the next seventy minutes "tone" continued to decrease slowly, after which it rose somewhat, but did not reach the control level at the time the experiment ended. Only the first hundred and ninety-five minutes of the postmedication period are shown in Figure 1.

Propulsive Contractions

The changes in the level of propulsive contractions following the administration of tincture of belladonna, 0.4 cc., and atropine, 0.45 to 0.6 mg., are shown for each test in Figure 2. It can be seen

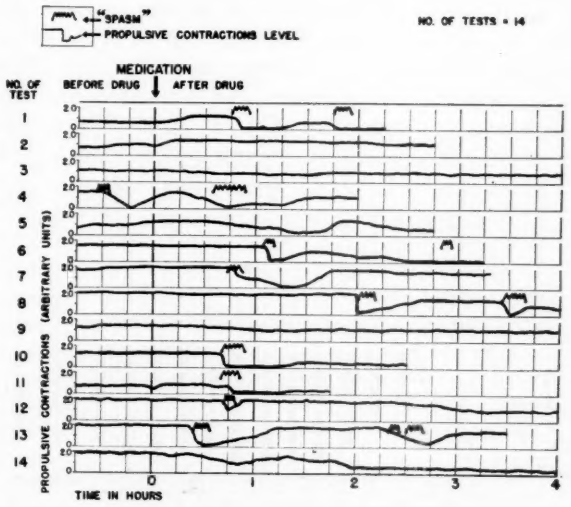

FIGURE 3. *Individual Graphs of the Variations in the Levels of Propulsive Contractions before and after the Administration of Placebos.*

The black lines indicate the summary values of the levels of propulsive contractions for the intestinal tracings in each test. Fourteen observations were made in 12 subjects. Tests 8 and 9 were carried out in one subject, and tests 10 and 11 in another. The graphs show that the rather abrupt diminution in propulsive contractions was almost always associated with the occurrence of "spasms" or temporary sudden elevations in "tone." The decrease in contractile activity was much less sustained than in the tests shown in Figure 2.

that twenty-five to forty-five minutes after the administration of tincture of belladonna, a striking diminution in propulsive activity occurred in all the tests except No. 6. Although test No. 6 showed a decrease in contractions twenty-five minutes later, it was suspected that it was a spontaneous decline occurring in association with a "spasm" or temporary sudden elevation of "tone" as indicated by the "saw-toothed" figure. Additional evidence that this subject showed no drug effect was suggested from his placebo test (Fig. 3, test No. 6), in which propulsive contractions decreased in association with a "spasm" at almost the same time as in the test with tincture of belladonna. After the initial decrease in propulsive contractions, the studies with tincture of belladonna showed a sustained reduction in activity two to four hours after the drug was given. These findings were in contrast to those observed in the placebo studies

(Fig. 3). Although 9 of the placebo tests showed a decline in contractions during the postmedication period* of twenty-two to seventy-five minutes, the latent period was much more variable than with the drug, and, more important, the decrease in activity was associated with "spasms" in 8 of the 9 tests. Furthermore, in most of the placebo studies there was a tendency for contractions to recover unless other "spasms" occurred.

Atropine was effective in reducing propulsive contractions except for test No. 12. Despite a gradual decline in contractions in this test the decrease in activity was not as clear-cut as in the other atropine studies. The latent period for the effect of atropine on propulsive activity was much the same as that for tincture of belladonna. Of the tests in which the drugs were regarded as having a posi-

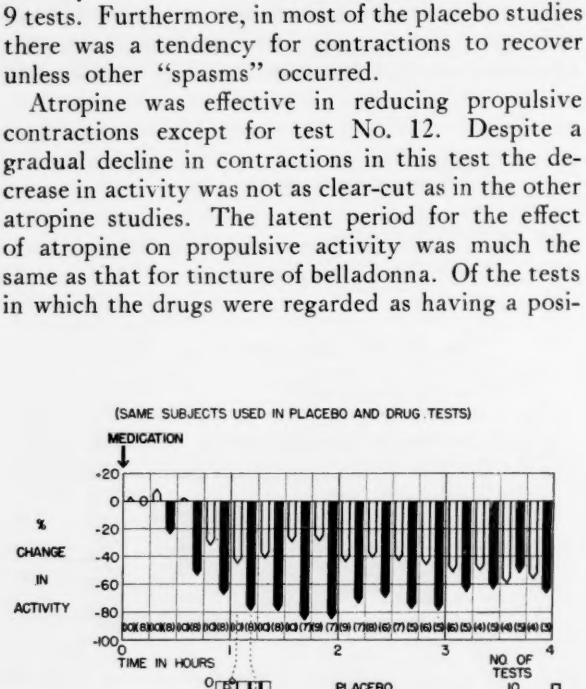
(SAME SUBJECTS USED IN PLACEBO AND DRUG TESTS)
MEDICATION
% CHANGE IN ACTIVITY
TIME IN HOURS
NO. OF TESTS
PLACEBO 10
ATROPINE 045-06 MGM. 3
TINCT. BELLAD. 04 CC. 5
INDIVIDUAL VALUES
NO. OF TESTS PER 15 MIN. + SEE( )

FIGURE 4. *Effect of Tincture of Belladonna, Atropine by Mouth and Placebos on Propulsive Contractions.*

The figure shows that tincture of belladonna and orally administered atropine caused a much more striking decrease in propulsive contractions than was noted after the administration of placebos to the same subjects. The white arrows (placebo values) and black arrows (drug values) indicate the mean of the sum of the percentage changes in activity in each subject for each fifteen-minute period compared to the last forty-five minutes of the control period. The individual variation in the placebo and drug studies for the postmedication interval of sixty to seventy-five minutes is shown by the scattergram.

tive action on propulsive contractions, the average time for the initial effect was twenty-three minutes, with a range of ten to forty minutes. For the remaining observation period the action of atropine was roughly comparable to that of tincture of belladonna. Test No. 14 was another example of the caution which had to be used in distinguishing a drug effect from a spontaneous decline in activity occurring after placebo administration. A comparison of this test with this subject's placebo study (Fig. 3, No. 14) revealed that contractions decreased in about thirty minutes in both. After the placebo was given, however, activity returned temporarily, and this fact was not observed in the atropine test for the same subject.

It will be noted that although the incidence of "spasms" was nearly the same in the drug and placebo studies, "spasms" did not seem to account for the rather sudden decrease in contractions in the tests with atropine and tincture of belladonna, except for the diminution in propulsive activity at the hundred-and-forty-two-minute postmedication period in test No. 9 (Fig. 2). In contrast, a reduction in propulsive contractions in the placebo studies was associated with the occurrence of "spasms" with the exception of tests No. 5 and 14 (Fig. 3).

Figure 4 shows the mean percentage decrease in propulsive contractions after the administration of atropine or tincture of belladonna as compared to the diminution in propulsive activity following the administration of placebos. Each subject had a placebo test as well as either one of the two drug studies. Because of the similarity in the actions of the two drugs, the tests with tincture of belladonna and atropine were considered as one group. In the first fifteen to one hundred and eighty minutes of the postmedication period propulsive contractions diminished on an average of 31 per cent in the placebo tests, as compared to 71 per cent in the drug studies. During the remainder of the postmedication period, the placebo tests showed an average decline of 54 per cent, and the drug studies an average decrease of 62 per cent. The range of variations in individual values in both groups of experiments is shown by the scattergram in the lower portion of Figure 4. It was found that the percentage change in propulsive contractions at sixty to seventy-five minutes after placebo administration varied from zero to –100 per cent whereas in the drug tests the variation was somewhat less, the range being from –20 to –100 per cent. Thus, it can be seen that for the first two hours, tincture of belladonna and atropine, 0.45 to 0.6 mg., diminished propulsive activity more than twice as much as the administration of placebos in the same subjects. During the next two hours the difference in the two groups was less striking, the drug effect being about 11 per cent more pronounced than the so-called placebo effects.

Total Contractions

The summary values for the levels of total contractions, before and after the drugs and placebos were given, are shown in Figure 5. Surface areas representing total contractions (propulsive and nonpropulsive) were uniformly measured for a five-minute period directly preceding each fifteen-minute interval and were expressed in square centimeters. These measurements indicated the same differences between the placebo and drug

*Whenever the term "postmedication period" is used in connection with the placebo tests, it indicates the period after the administration of the placebo.

tests as were indicated by the visual-inspection evaluation of changes in propulsive contractions alone. Total contractions after the administration of placebos decreased with the passage of time, but the percentage decline, compared to the average levels for the forty-five-minute premedication period, was less than that noted for the two drugs. The initial effect of the administration of atropine and tincture of belladonna was apparent within thirty minutes. The maximal effect of the drugs was first attained at sixty to seventy-five minutes in the postmedication period. At this time tincture of belladonna and atropine produced a 64 per cent decrease in total contractions compared to a 36 per cent decline in activity occurring after placebo administration. For fifteen to one hundred and eighty minutes of the postmedication period the two drugs caused an average decline in propulsive contractions of 61 per cent, as compared to a 28 per cent average decrease in the placebo

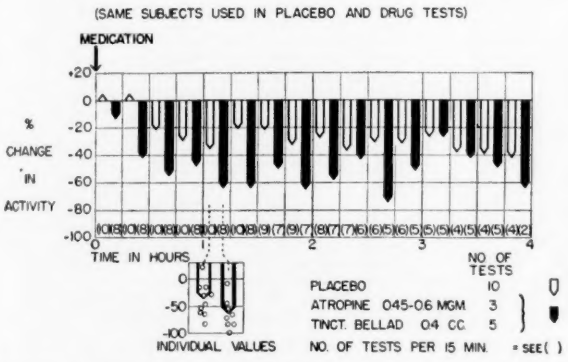
(SAME SUBJECTS USED IN PLACEBO AND DRUG TESTS)
MEDICATION
% CHANGE IN ACTIVITY
TIME IN HOURS
NO. OF TESTS
PLACEBO 10
ATROPINE 045-06 MGM. 3
TINCT. BELLAD 04 CC. 5
INDIVIDUAL VALUES
NO. OF TESTS PER 15 MIN. = SEE( )

FIGURE 5. *Effect of Tincture of Belladonna, Atropine by Mouth and Placebos on Total Contractions.*

The figure shows that tincture of belladonna and orally administered atropine diminished total contractions (propulsive and nonpropulsive) to a much greater extent than was noted after the administration of placebos to the same subjects. The mean values of the changes in activity for each fifteen-minute postmedication period were determined in the same manner as indicated in Figure 4. The values for the drug tests are shown by the black arrows, and those for the placebo tests by the white arrows. The range of the individual variation for the postmedication period of sixty to seventy-five minutes is shown by the scattergram. Total contractions were measured for five minutes previous to each fifteen-minute period in each test and were expressed in square centimeters of surface area.

tests. Thereafter, the differences in the two groups were not very striking. The individual variation in the percentage decrease in activity at sixty to seventy-five minutes is shown by the scattergram at the lower portion of Figure 5. The placebo values ranged from +21 to –83 per cent, whereas the drug values ranged from –7 to –100 per cent.

"Tone"

The changes in "tone," or sustained tension of the bowel wall, were much less striking than the changes in propulsive and in total contractions observed in the drug and placebo studies (Fig. 6). After the administration of placebos, "tone," except for forty-five to seventy-five minutes of the postmedication period, tended to be slightly elevated. The changes in "tone" averaged +7 per cent, with a range of –5 to +18 per cent from the thirty-minute interval to the end of the observation period. In the drug studies, on the other hand, there was a tendency for "tone" to be slightly decreased. The diminution in "tone" for the thirty

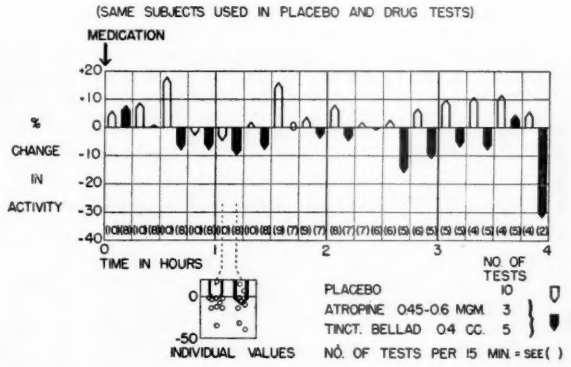
(SAME SUBJECTS USED IN PLACEBO AND DRUG TESTS)
MEDICATION
% CHANGE IN ACTIVITY
TIME IN HOURS
NO. OF TESTS
PLACEBO 10
ATROPINE 045-06 MGM. 3
TINCT. BELLAD 04 CC. 5
INDIVIDUAL VALUES
NO. OF TESTS PER 15 MIN. = SEE( )

FIGURE 6. *Effect of Tincture of Belladonna, Atropine by Mouth and Placebos on "Tone."*

The figure shows that "tone" was either unchanged or slightly reduced after the administration of tincture of belladonna and atropine by mouth, whereas "tone" tended to increase slightly after the administration of placebos to the same subjects. "Tone" was measured for five minutes previous to each fifteen-minute interval and was expressed in square centimeters of surface area. The percentage changes in "tone" were determined in the same manner as indicated in Figure 4. The range of the individual variations in "tone" is shown by the scattergram for the postmedication period of sixty to seventy-five minutes.

to two hundred and forty minutes of the postmedication interval averaged –8 per cent, with a range of +4 to –32 per cent. As shown by the scattergram in the lower portion of Figure 6, the range in the individual variation for the sixty to seventy-five minutes of the postmedication period was +18 to –34 per cent for the placebo tests and +14 to –40 per cent for the drug tests.

We concluded that in these subjects atropine and tincture of belladonna diminished "tone" only slightly. "Tone," under the conditions of these experiments, showed a tendency to remain slightly increased after the placebos were administered.

The findings revealed that atropine or tincture of belladonna was effective in decreasing propulsive and total contractions but produced only a minimal decrease in "tone." The summary data, which consist of the 14 placebo, 5 atropine and 9 belladonna studies, are shown in Table 1. The results for the first hundred and eighty minutes of the postmedication period were essentially the same

as the data already described in which each subject was tested with a placebo as well as with a drug. When the two drugs were compared, however, it was evident that tincture of belladonna consistently diminished "tone" to a greater extent than atropine did.

Changes in nonpropulsive contractions could not be expressed in quantitative terms either by the visual-inspection or by the surface-area measurements of the tracings. It was our impression, however, that nonpropulsive activity was decreased by the drugs although to a less extent than propulsive contractions. This opinion was substantiated in part by the fact that when the relative effects of the drugs and placebos were compared, tincture of belladonna and atropine decreased total contractions to a less extent than propulsive contractions alone. As previously mentioned, the measurements of total contractions included the nonpropulsive as well as propulsive contractions.

In general, the action of the drugs on each bowel segment studied was about the same. Analysis of individual tracing patterns revealed no difference in the effects of the drugs in 10 tests; in 4, there was slight evidence that activity in the proximal half of the duodenum diminished relatively less than in the more distal portions of the upper small intestine.

The only side effect noted after atropine or tincture of belladonna was moderate dryness of the mouth. This symptom was elicited in 5 out of the 14 subjects tested. There appeared to be no correlation between the presence of this side effect and the magnitude of the action of either drug on motor activity.

Discussion

By means of the multiple-balloon recording technic 14 observations have been made of the effect of atropine (given orally) and tincture of belladonna on the motility of the upper small intestine. The results were compared to the spontaneous changes in activity occurring in 14 tests after the administration of placebos. Marked individual variability in motor activity from subject to subject in certain instances and in a given subject from hour to hour was commonly observed. These variations and the relative difficulties in interpreting graphic records of motor activity make us hesitate to use statistical calculations in the assessment of the data until more observations have been made, particularly in the same subjects. In spite of these difficulties, we believe that the results warrant certain conclusions regarding the antispasmodic action of atropine and tincture of belladonna as investigated in this study:

Both drugs caused an initial decrease in propulsive contractions in an average time of twenty-three minutes, with a variation of ten to forty minutes.

The maximal decrease in propulsive and total contractions was first apparent seventy-five minutes after both drugs were given. The maximal effect persisted for the next forty-five to sixty minutes. Thereafter, activity recovered slightly. The decrease in propulsive and total contractions during the fifteen to one hundred and eighty minutes of the postmedication period

Table 1. *Summary Data of the Mean of the Sum of the Percentage Changes in Propulsive Contractions, Total Contractions and "Tone" for All the Tests after the Administration of Tincture of Belladonna (0.4 cc.), Atropine by Mouth (0.45 to 0.6 mg.) and Placebos.**

Interval after Medication	Propulsive Contractions						Total Contractions			
	After Belladonna		After Atropine		After Placebos		After Belladonna		After Atropine	
min.	*% change*	*no. of tests*	*% change*	*no. of tests*	*% change*	*no. of tests*	*% change*	*no. of tests*	*% change*	*no. of tests*
15	−1	9	0	5	+6	14	−9	9	−10	5
30	−33	9	−35	5	+11	14	−35	9	−41	5
45	−50	9	−70	5	−6	14	−65	9	−48	5
60	−76	8	−76	5	−30	14	−62	8	−57	5
75	−84	8	−80	5	−37	14	−71	8	−61	5
90	−87	8	−80	5	−33	14	−71	8	−57	5
105	−88	7	−83	5	−22	14	−55	7	−53	5
120	−86	7	−83	5	−21	13	−71	7	−56	5
135	−89	7	−76	5	−32	12	−71	7	−52	5
150	−74	6	−76	5	−31	11	−60	6	−47	5
165	−70	6	−76	5	−34	10	−68	6	−55	4
180	−70	6	−85	4	−39	8	−52	6	−51	4
195	−60	6	−85	4	−42	8	−52	6	−59	3
210	−59	6	−80	2	−35	6	−60	6	−49	2
225	−49	6	−75	2	−43	6	−56	6	−55	2
240	−48	5	−80	2	−41	6	−52	5	—	—

*In each test the average value for each 15-min. period was divided by the average value for the last 45 min. of the control period. The mean percentage change for any one group of tests was then obtained by division of the mean of the sum of the values per 15-min. period by the number of tests in that period.

was about 100 per cent greater on the average than the spontaneous decline in activity with placebos.

"Tone," or the resting level of contractions, was slightly decreased by tincture of belladonna and atropine, whereas in the placebo studies, "tone" tended to increase slightly with the passage of time. We were inclined to believe that in the dosages used tincture of belladonna was more consistent than atropine in reducing "tone."

The effects of the drugs on contractions are in essential agreement with the results of other workers.[8-12] Elsom and Drossner[8] found that 0.4 to 0.6 mg. of atropine given orally and 15 minims of tincture of belladonna produced an effect within thirty minutes and that the action persisted generally for ninety to one hundred and twenty minutes. We did not observe, as these workers did, that peristaltic or propulsive contractions were more pronounced before becoming diminished. We have, however, noted repeatedly in a few subjects a transient increase in "tone" and in the amplitude of segmental contractions that lasted nearly ten minutes after the intravenous injection of atropine, 0.3 to 0.6 mg.[14] Thus far, an insufficient number of subjects have been tested with atropine administered both orally and parenterally to determine the relative effectiveness of the drug given by the two routes. Because of the paucity of quantitative data in the literature, it was difficult to know how comparable our findings on changes in "tone" are to the results reported by others. We are inclined to agree with Huidobro et al.[9] and Posey and his associates[10] that atropine has little or no effect on "tone."

The quantitative differences established between the spontaneous changes in contractions noted after placebo administration and those obtained with the standard antispasmodic agents, atropine and tincture of belladonna, seemed important. With these studies as control observations, it was possible to demonstrate the relative ineffectiveness of the action of a number of drugs commonly used to diminish intestinal motility.[2]

Table 1 (*Concluded*).

Interval after Medication	Total Contractions		"Tone"					
	After Placebos		After Belladonna		After Atropine		After Placebos	
min.	*% change*	*no. of tests*	*% change*	*no. of tests*	*% change*	*no. of tests*	*% change*	*no. of tests*
15	+9	14	+2	9	+13	5	+4	14
30	−4	14	−4	9	+7	5	0	14
45	−22	14	−13	9	−11	5	+6	14
60	−33	14	−13	8	−12	5	−6	14
75	−28	14	−22	8	−6	5	−6	14
90	−22	14	−18	8	−6	5	0	14
105	−11	13	−11	7	0	5	+7	13
120	−23	13	−19	7	+5	5	+2	13
135	−23	11	−7	7	0	5	+2	11
150	−29	9	−10	6	0	5	+1	9
165	−30	8	−20	6	−8	4	−1	8
180	−16	8	−18	6	0	4	+5	8
195	−21	7	−17	6	+7	3	+5	7
210	−27	5	−14	6	+11	2	+8	5
225	−37	5	0	6	+9	2	+11	5
240	−40	4	−21	5	—	—	+4	4

Summary

The comparative action of atropine, 0.45 to 0.6 mg., given orally and tincture of belladonna, 0.4 cc. or 20 drops, on the motility of the upper small intestine in 14 healthy subjects is described. Motor activity was recorded with a multiple-balloon water-manometer system. The results are compared to similar studies with placebos.

Both drugs produced about a 100 per cent greater reduction in propulsive and total contractions than was observed after the administration of placebos.

"Tone," or the sustained tension of the bowel wall, was slightly diminished by tincture of belladonna. The results with atropine were not appreciably different from those noted with placebos.

Marked variation in motility from person to person and in a given subject from hour to hour would have made the assessment of drug effects difficult if placebo studies had not been used for the purpose of control observations.

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DERMATOLOGIC CLUES IN SURGICAL DIAGNOSIS*

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THE significance of dermatologic findings in the diagnostic study of a surgical patient has not been sufficiently felt. Textbooks of surgery and dermatology, alike, grant the subject only a few occult sentences. The literature reveals isolated bursts of attention, the most notable being Wiener's[1] excellent monograph on the general problem of skin manifestations of internal disease. It was with the hope of further stimulating interest in the subject that this review was prepared.

The purpose of this presentation is to review certain dermatologic clues that are of aid in surgical diagnosis. No mention is made of the many dermatoses that either require surgical treatment or are a direct extension of surgical problems — for example, spina bifida, maduromycosis, rhinophyma and scrofuloderma. Nor is an account given of the cutaneous lesions that are manifestations of systemic medical disease that may confront the surgeon.[2] It is rather the aim of this paper to review the cutaneous signs of internal surgical problems and dermatoses in which "surgical symptoms" may occur or in which systemic manifestations may pose rather direct surgical problems. Dermatologic descriptions are not given. For these reference is made to standard textbooks.[3]

What are the dermatologic clues that the surgeon must sense? To aid in presentation they have been grouped in four sections. The first group covers the cutaneous signs and symptoms of malignant tumors within the body. Of these, the truly specific manifestations are cutaneous metastases, which include bullae, macules, nodules, papules, Paget's disease of the nipple and tumors. Gates[4] in a study of 2298 malignant tumors, found that 2.7 per cent had metastasized to the skin. The metastatic lesion in the skin may be the very first sign of the tumor, appearing before lymph-node changes can be noted. These metastases are usually round, firm, painless papules and nodules,[5] frequently not recognized because of failure to examine carefully the disrobed patient. Especial attention should be directed to the umbilicus and scalp. The cutaneous lesions give no clue to the site of the primary lesion except for the fact that the earliest metastases appear in the general vicinity of the primary tumor — for example, a cutaneous metastasis from the uterus may first appear on the lower abdomen. In this connection, it is interesting to note that "seeding" of malignant cells may also occur in the surgical incision with resultant metastases in the operative scar. It must be stressed, however, that the gross appearance of metastatic lesions is not characteristic.[6] It ranges from that of a folliculitis to that of a large ulcerated tumor. Biopsy is necessary since it is the microscopical study that reveals the typical malignant cells representative of the source. On the other hand, biopsy never reveals the exact site of the primary tumor. Furthermore, recognition may be difficult in early lesions that show only inflammatory change due to destruction of the cancer cells by the skin.[7] The interval between the appearance of skin metastases and death is hard to predict. It may be years. However, the occurrence of ulceration is generally conceded to indicate an advanced stage of carcinomatosis.

Carcinoma is the most common of the malignant tumor metastases and such a metastasis may arise from a primary lesion in almost any part of the body. The route of spread is via the blood or lymphatics. The most common primary sites are the breast, stomach, lung, uterus and kidney. Reports reviewed by Gates[4] and others[1, 8-10] indicated the following other sites: tongue, tonsils, esophagus, jaw, thyroid gland, liver, gall bladder, pancreas, adrenal gland, ovary, intestine, pros-

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tate, urethra, penis, testicle and rectum. The type of carcinoma may also vary, adenocarcinoma, scirrhous carcinoma and epidermoid carcinoma being common.

Malignant melanoma usually arises as a primary growth in the skin and as such metastasizes elsewhere on the skin and in the body. However, malignant melanoma may arise as a primary lesion in the choroid coat of the retina, the central nervous system, the adrenal gland or even the mucous membrane of the intestinal tract. Accordingly, metastases from these internal sites are occasionally seen in the terminal stage of the disease.[11] This is exactly the reverse of the usual finding.

Lymphoblastoma or malignant lymphoma may also be considered as a malignant tumor with cutaneous metastases. It is a group composed of leukemia (lymphatic, myeloid and monocytic), Hodgkin's disease and lymphosarcoma. All these may show papules, nodules and tumors that result from a specific infiltrate of cells. Here again, biopsy, not gross appearance, makes the diagnosis possible.[1, 12] In addition, nonspecific skin changes (leukemids) that are entirely free from leukemic cells may occur.

Sarcoma and hemangioendothelioma[13] occasionally metastasize to the skin, presenting themselves as ulcerated tumors.

Paget's disease of the nipple is an eczematoid dermatitis that is indicative of carcinoma of the breast. Biopsy is necessary to distinguish it from other inflammatory dermatoses such as contact dermatitis. The presence of Paget's disease invariably demands a radical mastectomy. Hence, failure to recognize this condition deprives the patient of early effective surgical intervention.

In addition to the specific signs in the skin that point to internal cancer, there are many nonspecific signs. Although not nearly as significant as the specific signs, they are nevertheless of interest to the surgeon as relevant data to be weighed and analyzed. Acanthosis nigricans is the most remarkable of all of these dermatoses.[14, 15] Clinically, it appears as a dark, velvety, furrowed thickening of the skin, usually seen in the axillas and groins. It is not a neoplasm itself, yet in 1 out of every 2 patients its appearance ominously heralds an internal cancer. Although rare, its significance is measured by the fact that generally any adult with acanthosis nigricans may be assumed to have a highly malignant visceral cancer. Most often this is in the abdomen so that if a careful search fails to reveal evidence of a malignant lesion elsewhere, an exploratory laparotomy should be performed. In children the process, strangely enough, is usually without surgical significance, although in rare cases it may accompany a carcinoma.[16] Much remains to be learned about the mechanism of production of acanthosis nigricans.

Acne vulgaris of the face, chest and shoulders is seen to appear in the presence of tumors that lead to the overproduction of androgen in the body. Adrenocortical tumors are a good example of this type of lesion.[17, 18]

In addition to acanthosis nigricans and acne, which are special examples, many dermatoses may appear in association with internal cancer. The correlation is loose and examples rather rare, but reports in the literature listed in detail by Wiener[1] indicate that the dermatoses that may appear pursuant to a malignant tumor include dermatitis herpetiformis, dermatomyositis,[19] eczematous dermatitis, erysipelas, erythema multiforme, erythema nodosum, exfoliative dermatitis, herpes zoster, ichthyosis, acute lupus erythematosus, pellagra, poikiloderma vasculare atrophicans and urticaria. Local treatment for these tumor-induced skin changes meets with varying degrees of success. However, the lesions disappear upon complete surgical removal of the tumor.

Nonspecific cutaneous signs are also seen in patients suffering from a cancer. The pallor of anemia and the purpura of thrombocytopenia, both induced by cancer, are simple examples of this. A diffuse generalized pigmentation is also seen in advanced carcinoma. Dusky redness of the face and hands, as well as alopecia, acne, hirsutism and striae atrophicans, appear in patients with adrenocortical tumors[18] or a basophilic adenoma of the pituitary body (Cushing's syndrome). Any tumor may mechanically cause edema and distention of the veins. Pruritus is one of the common signs of internal malignant lesions. This may be localized or generalized. Intracranial tumors have occasionally led to pruritus localized to the nose. Tumors of the hypothalamus or surrounding structures may lead to generalized anhidrosis. Peau d'orange, or dimpling of the skin, is seen in an area over carcinoma of the breast. Other manifestations are striae atrophicans, ulcer and urticaria.

Attention should be directed to the fact that nonmalignant tumors also at times are associated with nonspecific skin changes. Examples are herpes zoster due to pressure of tumor; acne vulgaris, hirsutism and related symptoms as a manifestation of a benign adrenocortical tumor; pallor and hyperhidrosis in association with a pheochromocytoma of the adrenal gland; and edema and venous distention due to pressure of a mass on the veins.

In view of the absence of metastases from benign tumors, there are no specific changes in the skin. Yet the skin may present certain tumors or masses that reflect or are associated with systemic tumors or tumor-like masses. Neurofibromatosis, adenoma sebaceum and hemangioma are examples of developmental defects that randomly affect the entire body. The classic example of this is neurofibromatosis, which concurrently appears on the skin and throughout the body.[20] It may appear as

a tumor in the adrenal glands, the gastrointestinal tract, bones, brain and spinal cord, along nerves and elsewhere. Recently Welch, Ettinger and Hecht[21] reported an intrathoracic meningocele as occurring in association with neurofibromatosis.

Equally striking is the surgical significance of adenoma sebaceum, which is associated with generalized changes closely related to neurofibromatosis.[20] Here is a minor cutaneous change (for example, papules on the face) that diagnostically bespeaks powerfully the possible coexistence of a varied assortment of congenital malformations and tumors. The range of findings is great, as Butterworth and Wilson[22] showed in their classic review. The most commonly noted is tuberous sclerosis, presenting itself commonly as a tumor of glial tissue in the brain and manifesting itself in epilepsy and mental deficiency. Other changes in the brain have been microcephaly, plagiocephaly, hydrocephalus, atrophy and cysts. Retinal tumor, atrophy of the optic nerve and cataract occur rarely. Spina bifida and osteoporosis have been reported. Defects in the heart or vessels may be seen, as well as transpositions of the larger vessels. Visceral tumors may be widespread but are generally seen in the heart and kidneys. In this respect, Fish and McLaughlin[23] recorded the case of a patient with adenoma sebaceum who presented the surgical problem of recurrent abdominal pain, fever and anemia. Study revealed evidence of a renal tumor, which biopsy proved to be a liposarcoma. Nephrectomy was followed by complete recovery. Other renal tumors found have included angiomas, lipomas, hypernephromas, mixed cell tumors and neurofibromas. Rhabdomyomas of the heart are commonly seen. In addition, tumors and cysts have been found in the lungs, gastrointestinal tract, liver, pancreas, spleen, ovaries, bones, gall bladder, thyroid gland and breasts.[22] These have been shown to include myomas, fibromas, hemangiomas, lipomas, teratomas and dermoid cysts.

Hemangiomas of the skin have long been known to be an associative sign of hemangioma in the central nervous system. The classic example of this is the Sturge–Kalischer–Weber syndrome.[24] Essentially, it consists of a cutaneous angioma on the face, in association with atrophy and calcification of the cortex of the ipsilateral cerebral hemisphere. There is no angioma in the involved cortex, but there may be an overlying angiomatous meningioma. Clinically, the outstanding signs are epilepsy, contralateral hemiparesis and hemianopsia, ipsilateral exophthalmos and glaucoma. Attention has been largely directed to the hemangiomas of the face and brain, but it should be recognized that hemangiomas of the skin may be seen with hemangiomas of the spinal cord at the same level[25] or with hemangiomas of the gastrointestinal tract.[26] Apparently, this congenital mesodermal developmental defect is more often multiple than single. Rarely, angiomas are seen also in association with dyschondroplasia (Maffucci–Kast syndrome),[27] neurofibromatosis and adenoma sebaceum.

Kaposi's multiple idiopathic hemorrhagic sarcoma is another example of a systemic disease with its most conspicuous element in the skin. This is an angiosarcoma that produces tender, purplish nodules in the skin. Their presence should suggest to the surgeon the possibility of sarcomatous tumors of the gastrointestinal tract, mesenteric lymph nodes, liver, lungs, central nervous system and bones.[28] The skin simply mirrors the fact that nearly every organ in the body may be affected.

Endometriosis,[29] ganglioneuroma[30] and cysticerosis[31] are rarely seen in the skin, but when present may indicate systemic involvement. Moreover, many of the granulomas are but manifestations of internal masses of the same nature. Observations and interpretation of the skin changes here may alert the surgeon to the possibility of an internal granulomatous mass due to syphilis, tuberculosis, leprosy, sarcoidosis or coccidioidomycosis. The cutaneous xanthomas of Hand–Schüller–Christian disease may serve as a clue to the presence of other tumors in this condition, such as lesions of the orbit and skull.[32]

Finally, reference must be made to a dermatologic clue that points to the presence of intestinal polyposis. In an excellent paper Jeghers, McKusick and Katz[33] recently reported 10 cases of intestinal polyposis and associated melanin spots on the lips, oral mucosa and digits. Since the pigmentary patterning appears to be highly specific and distinctive, it should prove to be a valuable cutaneous sign of significance to the surgeon evaluating gastrointestinal problems.

Various surgical problems may have attendant dermatologic changes. Hyperthyroid patients often show a soft, oily skin, moist with perspiration, as well as urticaria. Rarely, hyperthyroid patients with exophthalmic changes exhibit localized areas of myxedema. These appear as elevated plaques or papules with a predilection for localizing on the legs.[34] They may occur before or after operation. Paradoxically, these islands of tissue show the same changes that are seen in the skin of a patient suffering from lack of thyroid function. Patients with chronic ulcerative colitis may present various pyodermic changes,[35] including massive, infected, ulcerative areas called pyoderma gangrenosum (gangrenous impetigo). This may result from the nutritional deficit suffered by these patients. In addition, erythema nodosum and nonspecific dermatoses may be seen.

Impetigo herpetiformis is a very rare pustular dermatosis that has been observed to follow parathyroidectomy.[3]

A dimple or a localized patch of hair in the sacrococcygeal area may indicate an underlying spina bifida occulta.

Injury to nerves may be manifested by sensory changes, hypohidrosis or hyperhidrosis and herpes zoster, or rarely by a neurotropic ulcer.

The final group of dermatologic changes of surgical note consists of conditions that cause or suggest the cause of surgical symptoms. Abdominal pain suggestive of a "surgical abdomen" may occur in at least four cutaneous conditions: the bite of the black-widow spider (*Latrodectus mactans*), erythema multiforme, Henoch's purpura, and herpes zoster. Arachnidism is at once the most striking and difficult to demonstrate. Although definite skin changes mark erythema multiforme and Henoch's purpura, it is worth while to state that herpes zoster of the abdomen may be not only associated with but also preceded by a continuous burning pain.

Dermatologic clues to the cause of abdominal pain are many and common. Some of them are discoloration (acute pancreatitis), the jaundice of biliary obstruction, the macules of infectious mononucleosis, typhoid fever and measles, the nodules of periarteritis nodosa, the petechiae of subacute bacterial endocarditis, the spider nevi of hepatic cirrhosis and the pigmentation of acute porphyria.[36, 37] Specific reference should be made to the paper on the Hofstätter–Cullen sign by Fallon and Manning.[38] On the basis of their work, it is evident that this cutaneous sign need not be blue, can appear elsewhere than at the umbilicus and is far from pathognomonic of extrauterine pregnancy. Probably, it can be caused by any condition producing colored intra-abdominal fluid. It was suggested that the pigments reach the skin by following ordinary fascial planes and openings.

Gastrointestinal bleeding may present a baffling diagnostic problem. Only rarely does the skin suggest the etiology, but it should be noted that patients with erythema multiforme, jaundice, Kaposi's idiopathic hemorrhagic sarcoma,[39] purpura, hereditary hemorrhagic telangiectasia[40] and systemic amyloidosis[41] may have gastrointestinal bleeding. The presence of melanin spots on the lips, oral mucosa and digits[33] points to gastrointestinal polyposis, in which bleeding may occur.

Pathologic fractures are rarely seen in association with cutaneous signs. However, they have been observed in syphilis (tabes dorsalis), tuberculosis, sarcoidosis, yaws, Maffucci syndrome (hemangiomas and dyschondroplasia[27]) and Albright's syndrome (osteitis fibrosa cystica with pigmentation of the skin[42]).

Summary

A review of dermatologic clues in surgical diagnosis is presented. It is focused on the dermatologic manifestations of internal tumors, dermatoses of especial surgical interest and dermatologic changes closely related to surgical symptoms.

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TRUE RENAL-ARTERY ANEURYSM*

Report of a Case

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ANEURYSM of the renal artery is an unusual lesion, only 90 cases having been reported in the world literature. Excellent reviews of the subject have been presented by Mathé[1] (1932), Howard, Suby and Harberson[2] (1941), Lowsley and Cannon[3] (1943) and Lazarus and Marks[4] (1944). The case reported below brings the total to 91.

ETIOLOGY

Renal-artery aneurysm may be "true" or "false," the latter constituting only 15 per cent of the total and representing essentially a spontaneously controlled hemorrhage secondary to rupture of the artery. A true aneurysm contains in its wall all the elements of the arterial wall and is caused by degeneration or inflammation of one or more of the layers. The various factors involved are not clearly understood.

The reported cases indicate that trauma is the most important cause, since slightly more than a third of the patients give a history of trauma. However, it is unlikely that trauma is the sole cause in more than a few cases. More tenable is the opinion that trauma is the precipitating factor for the aneurysmal dilatation of a vessel weakened by local or systemic factors.

It has been suggested that severe debilitating infections or inflammations of other systems may so weaken the wall of the renal artery as to render it readily liable to localized dilatation. Why this mechanism should ever be manifest in only the renal artery, sparing all the rest, is not clear. Renal-artery aneurysm has also been described in cases of periarteritis nodosa.

Richardson and Hyland[5] have shown that basal cerebral aneurysms are caused by congenital defects in the elastic tissue and media of cerebral arteries at the angles formed by arterial bifurcation. Similar defects may occur at the bifurcation of the renal artery.

Arteriosclerosis is a clearly recognizable cause in only about 15 per cent of cases, and syphilis in still fewer.

CLINICAL FEATURES

The ratio of males to females in reported cases is 4:3. The lesion occurs with equal frequency on each side. Approximately half the patients are between the ages of forty and sixty, but the age distribution is so broad as to be of little diagnostic value. The youngest reported patient was nine months, and the oldest eighty-two years of age.

Pain is the most prominent symptom, but is present in only slightly more than half the cases. When present it is usually a mild, dull, aching pain in the flank or upper abdomen. Rarely is it severe and colicky. Hematuria may occur if the aneurysmal sac perforates a calyx and establishes communication with the renal pelvis. Such hematuria is usually massive and often fatal. Hematuria may also result from occlusion of the renal artery, with infarction of the kidney, or from incomplete erosion of the renal pelvis by the aneurysm.

Tumor, of course, is recognized only when the aneurysm has reached a considerable size. The very large aneurysms are more likely to be traumatic; the largest is reported to have filled half the abdomen. The presence of pulsation or bruit in the flank is described in very few cases. One suspects that a bruit may be present more often than it is described, since most authors do not mention it. Obviously, when a renal-artery aneurysm ruptures, either spontaneously or as the result of violence, the clinical picture is immediately influenced by the extent and direction of the hemorrhage.

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The relation between hypertension and renal-artery aneurysm is interesting. Only 11 cases with hypertension are reported, and all these are found among the 56 aneurysms reported since 1920. The incidence of hypertension in these 56 cases, then, is 20 per cent. Only 3 of the 11 hypertensive patients were restored to normal blood pressure by nephrectomy.

X-Ray Findings

The diagnosis depends on characteristic x-ray findings. Calcification of the aneurysmal sac is the rule. This calcification is usually circular or wreath-like and is often incomplete. Its location in relation to the kidney is an important diagnostic feature. It lies anterior to the pelvis, medial to the kidney and opposite the upper third of the kidney. If the aneurysm is large enough to displace the kidney, it will move it laterally and may produce a pressure deformity, which will be apparent first in the upper major calyx. The lesion should be localized as accurately as possible by oblique and lateral as well as conventional anteroposterior films. Renal arteriography by injection of a contrast medium into the aorta has rarely been used.

Treatment

Treatment has been nephrectomy, including excision of the aneurysmal sac. Since the danger of sudden fatal hemorrhage from rupture of the sac is considerable, it is mandatory to correct or remove the lesion once the diagnosis is made. Death occurred in all reported cases in which operation was not performed. Of 41 patients operated on since 1920, 5 died — a mortality of 12 per cent. In 3 of the 5 fatal cases the operation was performed as an emergency procedure after hemorrhage had already occurred.

Under ideal circumstances it may be possible to excise or repair the aneurysm and conserve the kidney. Only 4 such cases have been reported. Orth[6] found a rather large traumatic aneurysm, which he was able to dissect away from the renal artery, suturing the original rent in the side of the artery. The patient of Callahan and Schiltz[7] had a smaller aneurysm arising like a diverticulum from one side of the renal artery, and they were able to amputate the aneurysm and suture the rent in the side of the artery. The case reported by Gorro and Baques[8] and that reported by Mathé[9] were small aneurysms of a branch of the renal artery. In both cases the aneurysm was excised, and the continuity of the involved branch was permanently interrupted. Wiring of the aneurysmal sac and excision of the aneurysm, with restoration of the continuity of the artery, have not been reported.

Case Report

T. F. S., a 32-year-old machine operator, was admitted to the hospital on March 29, 1948, complaining of pain in the left flank of 2 weeks' duration. The pain was dull and gnawing and was localized to the costovertebral angle and upper flank. There was no history of previous renal disease. He could recall no trauma to the back or abdomen. During the week before admission he had experienced slightly increased frequency of urination. There was no history of hematuria, chills, fever or venereal disease.

At the age of 9 the patient had had "rheumatism" of sufficient severity to confine him to bed for 4 weeks. This was complicated by a "leakage of the heart," which persisted until the age of 15. Since then he had been active, had engaged in athletics and had served a tour of active duty in the Army without cardiovascular symptoms. Approximately 2 years prior to this admission the patient was examined at the hospital because of a sore neck. X-ray films of the lumbar spines taken at that time are discussed below.

Physical examination showed a well developed, healthy-looking man of medium height and build. The blood pressure on admission was 180/100, but many subsequent readings before operation ranged between 120/80 and 140/90, throwing considerable doubt on the validity of the first reading. The remainder of the physical examination was negative. The heart was not enlarged, the pulse was normal, and there were no murmurs. The kidneys were neither enlarged nor tender. No abdominal organs or masses were palpable. The internal and external genitalia were normal. There was no evidence of disease of the peripheral vessels.

A complete blood count was normal. The urine was grossly clear, with an acid reaction, a specific gravity of 1.008, and negative tests for albumin and sugar. The urinary sediment showed no red cells, pus cells, casts or organisms. Urine culture was sterile. The blood urea nitrogen was 10.0 mg. per 100 cc. The phenolsulfonphthalein test showed 60 per cent excretion of the dye in the first and 30 per cent in the second hour. The blood Mazzini reaction was negative. The serum calcium was 9.3 mg., the serum inorganic phosphorus 4.3 mg., and the serum alkaline phosphatase 4.0 Bodansky units per 100 cc.

Posteroanterior and lateral chest films were normal. Retrograde and intravenous pyelograms, using left posterior oblique, left lateral, and anteroposterior projections, demonstrated a round, apparently spherical mass 6 cm. in diameter just medial to the upper pole of the left kidney. This mass was incompletely outlined by curvilinear areas of calcification. The left kidney was noticeably displaced laterally. There was evidence of extrinsic pressure on the upper portion of the left renal pelvis and upper major calyx. The lateral and oblique projections showed the mass to lie immediately anterior to the renal pelvis, displacing the pelvis and upper major calyx somewhat posteriorly. X-ray films of the lower extremities revealed no calcification of the vessels. (The single x-ray film of the lumbar spines taken 2 years previously had disclosed the same, partially calcified mass in the left upper quadrant, two thirds the size of the present mass and a little nearer the midline; the lesion had apparently not been noted at that time, and no further diagnostic measures had been taken.)

At operation, under endotracheal cyclopropane anesthesia supplemented by Pentothal sodium and curare, the kidney was exposed through an extraperitoneal incision in the left flank. The organ itself was grossly normal. In the region of the vascular pedicle was a large, vigorously pulsating mass, roughly spherical, pearly gray in color, and about the size of a tennis ball. Calcified plaques were palpable in its wall. The mass was adherent to the abdominal wall posteriorly and to the aorta medially. With some difficulty a short segment of normal renal artery about 1 cm. in length between the aorta and the mass was exposed. This segment was clamped, and the kidney was excised with the mass after the ureter had been cut and ligated.

The pathological report* was as follows:

> The kidney is normal in size and gross appearance. At the hilus there is a cystic mass, 6 by 6 by 4 cm., representing an aneurysmal dilatation of the renal artery. Immediately adjacent to this is a smaller mass, 2 by 2 by 2 cm., which communicates with the larger sac by a 5-mm. channel. From the smaller sac three small branches of the renal artery enter the kidney. The medial aspect of the upper

*We are indebted to Dr. Raymond Yesner for the description and discussion of the pathological findings.

pole of the kidney is flattened as though by pressure from the adjacent aneurysm (Fig. 1).

Microscopical examination of numerous sections of the aneurysm shows the intima to be thickened and edematous. The greatest change, however, is seen in the media, where there is fibrosis and increased vascularity with scattered areas of calcification. There is fatty infiltration of the muscle fibers and foci of cholesterol deposition. The adventitia shows only a few lymphocytes and plasma cells and some inflammatory reaction around blood vessels. Section of the kidney itself shows nothing abnormal.

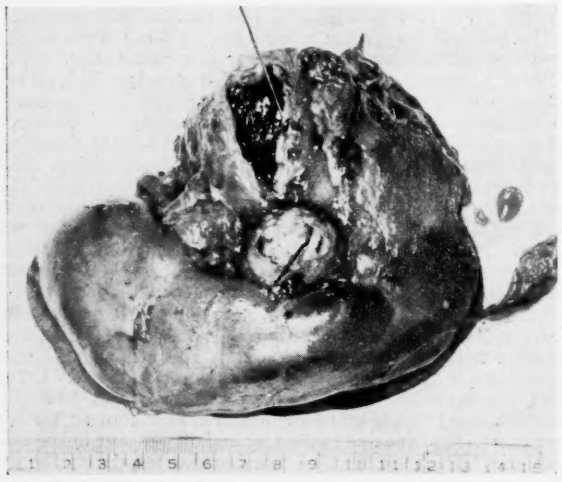

FIGURE 1. *Photograph of the Excised Kidney.*
The probe is seen entering the larger aneurysmal sac and leaving by way of the smaller sac.

The most striking histologic change was the extensive degeneration of the media, not characteristic of idiopathic medionecrosis, and greater than could be accounted for by degeneration beneath arteriosclerotic plaques. The arteriosclerosis was probably secondary to the medial damage.

Half the kidney and artery was forwarded to the Army Institute of Pathology, where the material was coded as arteriosclerosis and atypical necrosis of the media, with aneurysm of the renal artery.

It is tempting to speculate about the nature of the illness that the patient claimed to have had at the age of 9, particularly regarding the possibility of its having been low-grade periarteritis or some other vascular disease of which this aneurysm was a sequel.

The postoperative course was uneventful. The wound healed promptly without complication. The phenolsulfonphthalein test postoperatively showed 50 per cent excretion in the first and 10 per cent in the second hour. The blood pressure during convalescence remained at 120/80. The pain in the left flank was relieved.

CONCLUSION

This case offered the unusual opportunity to observe the growth of a renal-artery aneurysm during a two-year period. During that time the lesion increased in size by about 50 per cent without producing any noteworthy symptoms until two weeks before the patient was seen. This feature is a helpful point in the differential diagnosis and supports the likelihood of an unfavorable prognosis in cases in which the lesion is not treated.

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A CORRECTIVE SHOE FOR TOE DROP

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PARALYSIS of the muscles below the knee is the most frequent residual defect following infantile paralysis. For this defect many surgical procedures are available, and many more various mechanical aids have been devised. The interest of this article is limited to the explanation of a mechanical aid for toe drop whether due to poliomyelitis or other nerve injuries.

Some type of metal appliance is usually recommended, all of which have the same weaknesses. The chief disadvantage is that all create pressure points on the skin of the leg, producing tenderness by friction if the ankle is permitted to move.

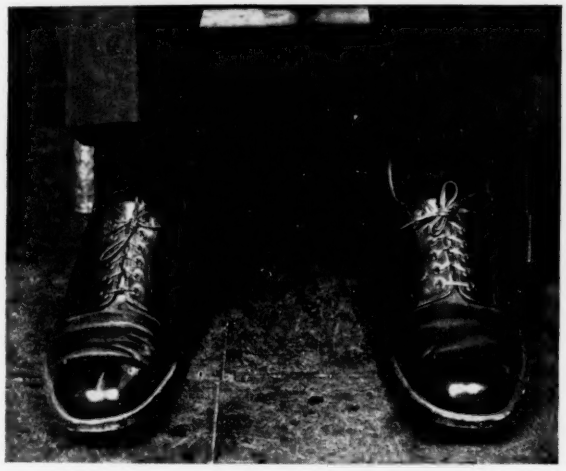

FIGURE 1. *Photograph Showing the Appearance of the Shoe in the Normal Standing Position.*

Another drawback is that if the ankle is held rigid, strong steel is required and a lock joint used so that the foot cannot be extended on the leg, and this makes an awkward motion and a pounding sound with each step. A spring type of brace is either too flexible to be effective or so strong and rigid that the metal bends unevenly, and at the point of greatest flexibility crystallization develops and the finest steel breaks in two or three days of much wear. The shoe described below overcomes the need for metal and has the aesthetic advantage of neatness (Fig. 1) at least for men (a shoe has not yet been made for women).

A personal need existed as the inspiration for the designing of this shoe and not any special interest in orthopedics. A toe drop resulting from infantile paralysis at eighteen years of age stimulated a search for any help that would make unnecessary lifting of the left knee higher than the normal right

FIGURE 2. *Photograph Showing How the Stiff Counter Was Cut Out to Avoid a Pressure Point on the External Malleolus. This is a very important part of the shoe, but the adaptation is easily accomplished.*

leg so that the toe would not drag. The evolution of this shoe was possible because interested shoe and leather executives co-operated completely with the patient without selfish motives.

FIGURE 3. *Photograph, Showing a Superimposed Negative on Negative, Demonstrating the Effectiveness of the Shoe in Elevating the Toe Out of Its Dropped Position.*

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The first shoe used was an unfashioned high boot for both feet. Because of the marked muscular atrophy the left boot could not be laced tightly and was therefore only partially successful in accomplishing its purpose of keeping the foot at right angles to the long axis of the leg.

This shoe was shown to the first interested leather men, one of whom had his patternmaker fashion the left boot to the ankle so that it could be laced tightly. This was a great improvement but presented the disadvantage of becoming too tight around the ankle when much walking was attempted. This disadvantage was overcome by placing the eyelets for lacing increasingly far apart beginning from the toe. This improved model also had a major fault: when the leg moved on the foot the upper shoe had to move on the foot of the shoe. The constant flexing of the leather weakened the stiffness so that the shoe soon failed in its purpose of lifting the toe.

The third major improvement and the present shoe (Fig. 1 and 2) consisted in setting the pattern forward on the base and leaving the front open except the lacing that is present in an Oxford type of shoe (Fig. 2).

The shoe illustrated in the photographs (Fig. 1-3) is the acme of all appliances for toe drop that this patient has worn. It holds the toe at the correct angle for comfortable walking, there are no pressure points, it is neat in appearance, and it corrects the exceedingly uncomfortable feeling of a flail foot (Fig. 3). This shoe has not been used when a marked lateral instability is present and might need modification.

47 Bay State Road

MEDICAL PROGRESS

ABDOMINAL SURGERY

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THE great volume of literature devoted to abdominal surgery continues unabated, and it is therefore possible, in this brief survey, to include only the salient features of articles that are of great importance or of wide interest. During the past year, surgeons generally have been concerned with more accurate appraisal of the value of established procedures rather than the introduction of new operations. Of particular interest, in this respect, are the management of acute massive gastrointestinal hemorrhage, the treatment of the various lesions of the pancreas and the surgical therapy of polyps and cancer of the colon and rectum. These problems are discussed under the appropriate headings.

GENERAL CONSIDERATIONS

Gas

A most interesting series of clinical experiments on the determination of the source of gastrointestinal gas is described by Maddock, Bell and Tremaine.[1] They found that the major source is external air entering the esophagus because of a relaxed superior esophageal sphincter. Air was found to pass very rapidly through the gastrointestinal tract and when aspirated into the stomach of experimental subjects reached the cecum in an average of fourteen and six-tenths minutes and was passed as flatus in thirty minutes. Patients under pyelography did not accumulate gas if continuous gastric suction was used, and in the others, the nervous patients had three times as much air aspirated from their stomachs as the calm ones.

Oxycel

Although oxycel has proved of value in many cases of hemorrhage, indiscriminate use is hazardous since it is a foreign body susceptible to infection. Vanderhoof and Merendino[2] found 3 unfavorable reactions in 4 patients on whom it had been used in the gall-bladder bed after cholecystectomy. Hinman and Babcock[3] and Uhrich[4] have presented experimental evidence that particles of oxidized cellulose promote the growth of bacteria in the infected peritoneal cavity of dogs, or nephrectomy incisions in rabbits.

Situs Inversus

Situs inversus occurs once in every 6000 to 8000 persons. Blegen[5] has collected the available literature, which includes records of 144 patients with 158 operations. Transposition was complete in 125 cases and partial in 19. False projections of pain to the opposite side of the body was present in at least 33 per cent of the cases of left-sided appendicitis and in 8 per cent of left-sided gall-bladder disease.

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Antibiotics

Altemeier[6] has studied 598 cases of acute septic peritonitis in the past six years in the Cincinnati General Hospital and concludes that success depends primarily on early diagnosis and good surgical intervention and secondarily on chemotherapy and adequate supportive therapy. However, a reduction of 60 per cent in mortality compared with a control group is apparently due to the effect of chemotherapy. Lyons[7] advises the daily administration of 1,500,000 units of penicillin, 0.75 to 1.5 gm. of streptomycin and enough sulfadiazine to maintain a blood level of 5 mg. per 100 cc.

Aureomycin has not yet been used widely enough for clinical assessment of its value. However, in a comparison of the newer antibiotics in experimental peritonitis in dogs, Yeager and Ingram[8] found a survival rate of 20 per cent in the control animals compared with 60 per cent for those treated with streptomycin and 90 per cent for those treated with aureomycin. Chloramphenicol (Chloromycetin) shows suggestive evidence that it may have comparable value in peritonitis.

The preoperative preparation of the colon by oral administration of streptomycin has been investigated by Lockwood et al.,[9] who found that the reduction in intestinal flora was unpredictable and unreliable. In cases showing a favorable early response, the organism rapidly develops resistance to the drug.

Ambulation

Drye[10] inserted balloons at the time of operation and found that in the supine position the intraperitoneal pressure is equivalent to about 8 cm. of water in both the lower and upper abdomen. In the erect position pressure in the lower abdomen rises to only 20 cm., whereas coughing and vomiting raise it to 80 cm. This offers evidence that early ambulation does not produce undue tension on the abdominal wound.

Intestinal Intubation

A complete summary of the various intestinal tubes may be found in Cantor's[11] monograph. Wild[12] has described his own modification of the Miller–Abbott tube, laying emphasis on the necessity of using two terminal holes placed just distal to a balloon bolus for good results. Chaffee[13] has collected the complications referable to these tubes; they are important enough to be listed in full: sinusitis and otitis media; esophageal stricture; laryngeal obstruction; knotting of the tube; rupture of esophageal varices; ruptured viscera; inability to withdraw the balloon-tipped tube; and breakage of the mercury-filled bag. The warnings he sounds are so important that they are repeated — namely, the tube is removed if the patient presents dyspnea, dysphagia, hoarseness, blood-streaked sputum or croupy cough; the position of the tip of the tube is changed daily; nasal intubation is avoided in patients with sinusitis and head colds; gastric intubation is not used in patients with esophageal varices; the tube is removed as soon as it has completed its mission; and tubes are not permitted to pass the ileocecal valve, but, if they do, they should be cut off and allowed to pass by rectum.

Stomach and Duodenum

Acute Massive Hemorrhage

The large number of papers on this subject indicates that there is a more active interest in this problem in various surgical clinics, and that more patients are being managed by early surgery. If surgery is to be employed in these cases, there must be prompt diagnosis by a combined medical and surgical team to exclude, as far as possible, bleeding from esophageal varices, gastritis or blood dyscrasias. There must also be rapid blood replacement, adequate anesthesia and excellent surgical technic. If any of these essentials are lacking, it is best to treat the patient by adequate blood replacement and dietary measures. Either method will show results far better than those in the past.

The value of adequate prompt blood replacement alone is shown by Costello,[14] who reports a reduction in mortality from 25 to 4 per cent in the treatment of "massive" hemorrhage (exact amount of bleeding undetermined) from all causes by this method; he gave 3 or 4 liters of blood during the first twenty-four-hour period when necessary. The value of conservative therapy is also analyzed by Pedersen,[15] who studied 850 cases of bleeding peptic ulcer (any type of gross hemorrhage is qualified for inclusion) in the Copenhagen Hospital from 1938-1948. Meulengracht's[16] principle of prompt, free and frequent feeding and blood transfusion is now employed. The over-all death rate was 3.5 per cent, which is higher than that of Meulengracht, who used the same data up to 1946, because older patients are now appearing in the hospital.

All students of the problem have agreed that some patients with bleeding ulcer cannot be saved unless operated upon. This has become particularly true in the large hospitals when numerous bleeders often deplete the bank of rare types of blood. Whether it is possible or not to pick out the particular patients who will do poorly under conservative measures is the essential feature of the problem. Stewart[17] has investigated the method of indiscriminate operation on all patients with true massive hemorrhage from gastric or duodenal ulcer, and has obtained the enviable operative mortality of 3 per cent, as compared with 29 per cent in those treated conservatively.

It is considered possible to select the group of patients that require immediate or early operation.[18]

Patients who fail to stop bleeding after entry (and they are nearly all fifty years of age or over) or those who have a recurrent hemorrhage under observation should be operated on as soon as the best facilities are available. Others are subjected to interval gastrectomy. This principle of selective surgery is also approved in the recent papers of Amendola,[19] Sullens, Steigmann and Meyer,[20] Warthin, Warren and Wissing,[21] Fraser and West,[22] Daly, Johnston and Penberthy[23] and Lewison.[24] Although the exact indications for surgery are somewhat changeable in various clinics, the results obtained do not differ greatly. We found, in a total of 113 operations for massive hemorrhage from ulcer, that operations done immediately or on the first recurrence of hemorrhage carried a mortality of 10 per cent, that surgery after repeated recurrences was fatal in 57 per cent and that interval operation was done with a 2 per cent mortality.

Vagotomy

A large number of articles have appeared on the experimental and clinical effects of vagotomy. Although most surgeons have found the results more disappointing with the passage of time, continued optimistic statements come from Dragstedt and Camp[25] and Crile et al.[26] Crile reports that vagotomy, in conjunction with gastroenterostomy or pyloroplasty, has given better results than gastric resection or gastroenterostomy alone. Failure occurred with vagotomy in only 6 per cent, with gastroenterostomy in 50 per cent and with resection in 19 per cent. Dragstedt[25] observed excellent results in 80 per cent of cases of transthoracic and 88 per cent of transabdominal vagotomies (not combined with other operations), and the majority of patients with unsatisfactory results had entire relief by subsequent gastroenterostomy. On the other hand, vagotomy alone gave only 50 per cent satisfactory results in Grimson's[27] hands, and Healy and Sauer[28] found complete relief of symptoms in only 20 per cent of patients treated by vagotomy alone.

It is clear that gastric ulcer fails to respond well to vagotomy because hypersecretion of neurogenic origin is not present; thus, Dragstedt's[29] and Grimson's[27] experiences have both been unsatisfactory. It seems logical that cases of duodenal ulcer selected for vagotomy should also vary in their response, depending on the relative preponderance of humoral or vagal elements in gastric secretion. Griswold[30] notes that although both types of gastric stimulation produce high acid, pepsin content is low with humoral secretion, and high with vagal. On this basis, he attempts to determine which patient should be treated by gastric resection and which by vagotomy.

It therefore seems probable that vagotomy in combination with some other procedure will finally have some place, not yet determined accurately, in the treatment of duodenal ulcer. As a concomitant procedure, besides those of pyloroplasty and gastroenterostomy mentioned above, Fallis and Barron[31] have tried a Von Haberer–Finney gastrectomy, and many others a subtotal gastric resection. The results have usually been less satisfactory than with resection alone, because of side effects of the vagotomy. The whole subject has been very well reviewed by Trimble and Lynn.[32]

Gastric Resection

Meanwhile, the results of large series of gastric resections are being reported in detail. Mayo,[33] in an able and encyclopedic review of the whole ulcer problem, concludes that a subtotal gastric resection offers the best long-term results of any operation in use at present in the elective surgical treatment of benign gastric and duodenal ulcer. The procedure of choice appears to be a resection of three fourths or more of the stomach, including the pyloric mucosa, with a Hofmeister type of gastrojejunal anastomosis made as close as is technically possible to the duodenum.

Gaviser[34] has evaluated all patients with duodenal and gastric ulcer operated on from 1940 to 1945 in the University of Minnesota Hospital. All were treated by a 75 per cent resection. There was a recurrence rate of less than 1 per cent, and only 2.6 per cent of patients had symptoms of a dumping syndrome. Sixty-one per cent were able to eat all foods without restriction, and 34 per cent took a regular diet but had difficulty with a single meal. Wells and Brewer[35] report the British experience, stating that after a personal experience with 363 patients "following subtotal gastrectomy, the results have been satisfactory in so near to 100 per cent of the cases that it is believed the operation may be recommended with the maximum confidence and a minimum of guarded reservation with which it has in the past been necessary to approach the subject."

The dumping syndrome that occurs occasionally after gastric resection has been studied by Machella.[36] He reproduced the symptoms in normal as well as gastrectomized patients by the intrajejunal instillation of hypertonic solution of glucose, protein hydrolysate and sodium sulfate and by distention of the jejunum with an air-inflated balloon. He suggests that these symptoms are due to distention of the jejunum by fluid, which enters the lumen of the gut from the blood stream in response to a hypertonic solution. Adlersberg and Hammerschlag[37] described the "postgastrectomy syndrome," attributing the symptoms that appear within the first half hour to mechanical causes, and the late symptoms, appearing two or three hours after eating, to an exaggerated postprandial hypoglycemia.

Ulcer

Several interesting reports of various types of ulcers have appeared. Wangensteen and Leven[38] believe that esophagitis is a manifestation of ulcer disease and cite 6 cases of esophagitis or esophageal stricture, or both, that were relieved by gastric resection alone. Mason and Pollard[39] found 13 cases of peptic ulcer after 1498 splanchnicectomies for hypertension. Since there was complete or nearly complete abolition of normal pain sensation, the complications were often serious. A series of 81 cases of anastomotic ulcer were studied by Ransom[40] at the University of Michigan Hospital. Of 106 previous operations on the stomach, 60 were gastroenterostomies, and 7 gastric resections. He believes that an adequate gastric resection for anastomotic ulcer is the treatment of choice but that if this has already been done, a vagotomy should be carried out.

Cancer

A reduction in mortality from total gastrectomy is apparent. Scott and Longmire[41] report a mortality of 3.3 per cent in the last two years, and Wangensteen[42] one of 3.5 per cent. The debate continues over the wisdom of routine total gastrectomy for cancer. Longmire reports a group of 63 total gastrectomies performed in the Johns Hopkins Hospital from 1944 to 1949. Of the 55 cases done for cancer, 30 might have been treated by partial gastrectomy, but the total operation was elected since the surgeon cannot judge accurately the extent of invasion of the gastric wall or lymph nodes by tumor. Wangensteen ascribes his low mortality to buttressing of the jejunal wall against the posterior wall of the esophagus, and temporary suction drainage of the left subdiaphragmatic area.

We agree with Zinninger and Collins[43] that routine total gastrectomies for cancer of the stomach should not be used because of marked feeding difficulties after many such operations. They believe that a frozen section of the cut margin at time of operation may be of importance to determine if an adequate operation has been done. In cancer near the pylorus, 30 per cent of cases showed cancerous invasion of the duodenum. With cancer of the cardia, the greatest length of microscopical invasion of the esophagus beyond the apparent edge of the tumor was 25 mm. in their cases.

The combined abdominothoracic incision is finding increased favor in many clinics[42, 43] in certain cases of total gastrectomy when exposure of the esophagus is difficult.

Gall Bladder

The Silent Gallstone

In an attempt to determine the fate of the patient with the silent gallstone, Comfort, Gray and Wilson[44] sent letters to 184 patients who had had silent stones discovered in the Mayo Clinic at least ten years before. Unfortunately, only 62 per cent answered the letter, but it was determined that of the 112 who replied, 51 had symptoms, cholecystectomy was necessary in 24, and 3 died postoperatively. None were known to have developed cancer.

Arminski[45] has reviewed the literature very completely in an attempt to determine the incidence of cancer of the gall bladder. He believes the incidence of cancer with cholelithiasis is 3 per cent. In over 20,000 autopsies, the incidence of cancer of the gall bladder was 0.4 per cent, and stones were present in 75 per cent of these cases of cancer.

When the silent stone in the functioning gall bladder is followed by such a high incidence of symptoms and by a cancer rate that is more than the expected mortality rate of elective cholecystectomy, the argument for the removal of silent stones becomes even stronger. We must reaffirm the previously expressed dictum that cholecystectomy is indicated for silent stones except when express contraindications are present.

On the other hand, the distressing frequency of postoperative stricture of the common duct is apparent. Cholecystectomy should not be attempted unless the surgeon is well trained, anesthesia is good, assistance is adequate and good lighting is present. Walters and Phillips[46] believe the incidence of stricture has risen since the war. The results of repair are poor enough in the best hands; the occasional surgeon should not attempt such a procedure. Walters[47] prefers a biliary duodenal anastomosis, with splinting tubes of polythene left in place for at least three and possibly for twelve months. He believes 60 per cent of the cases can be cured by the first operation. The others have further symptoms or operations. Lahey[48] prefers an end-to-end anastomosis of the duct after isolation of the transpancreatic portion.

Longmire and Sanford[49] have given a later report on the use of intrahepatic cholangiojejunostomy. In 4 cases it was possible to make a satisfactory anastomosis in all. One patient has been well for a year, 2 are greatly improved, and 1 died of homologous serum hepatitis. Wilson and Gillespie[50] have modified this procedure, using a Roux anastomosis to the liver.

We believe that a Roux anastomosis of the jejunum to the stump of the common duct is the most satisfactory operation yet devised. The main problem consists in retention of polyethylene splint for a long enough period after operation.

Pancreas

Acute Pancreatitis

The treatment of acute pancreatitis has usually been considered to be nonoperative, since spon-

taneous recovery is the rule if pancreatic edema only is present, and operation has appeared to hasten death when the hemorrhagic variety occurs. For the control of the severe pain, Ochsner[51] has recommended a novocain block of the greater splanchnic nerves. However, it is of interest that Rhoads[52] has revived the operative treatment of acute pancreatitis. Cholecystostomy and wide drainage of the pancreas have been carried out in all severe cases, with an over-all mortality of 3.2 per cent. He ascribes the remarkably low death rate to the large doses of penicillin used postoperatively.

Recurrent Pancreatitis

The treatment of recurrent episodes of acute pancreatitis has been approached by Doubilet and Mulholland,[53] who do a blind section of the sphincter of Oddi with a special instrument, believing that spasm of the sphincter leads to intrapancreatic regurgitation of bile, with the production of acute pancreatitis. Gray et al.,[54] after division of the sphincter of Oddi in dogs, found that duodenal contents regurgitated into the gall bladder, producing chronic cholecystitis and occasionally hepatitis. These results, in addition to the danger of hemorrhage, we believe, make it wise to consider this particular operation with some caution.

Various other operations are available for chronic or recurrent pancreatitis. They include removal of pancreatic calculi from the ducts, ligation of the pancreatic duct, partial or even total pancreatectomy and splanchnicectomy. Of these procedures, the one most likely to be successful is splanchnicectomy. Ray and Console[55] have studied 5 cases in which the operation was performed. They conclude that the minimal operation thus far found to provide total analgesia of the pancreas is bilateral resection of the ganglionated chains from the eleventh thoracic to the first lumbar segment and of the lowest 8 cm. of the greater splanchnic nerve. In some patients, unilateral sympathectomy may be sufficient to afford relief of pain. The operation is of limited value in carcinoma of the pancreas chiefly because of the tendency of the disease to spread outside the organ to pain-sensitive areas supplied by somatic sensory nerves. For the same reason, sympathectomy occasionally fails for pancreatitis. Thus, Bogle[56] reports a case of pancreatic calculosis unrelieved by sympathectomy that finally responded to subtotal pancreatectomy.

Our experience in the Massachusetts General Hospital with 5 patients subjected to sympathectomy for this cause has been that 2 with bilateral denervation did well, and 1 had complete relief after a unilateral operation. Two others have had recurrent symptoms after a unilateral denervation. Total pancreatectomy has led, in 2 cases, to incapacitating metabolic problems.

Cancer of the Pancreas

Radical pancreatoduodenal resection has now been employed widely for the treatment of cancer of the ampulla of Vater, pancreas and duodenum. An appraisal of 61 cases is given by Cattell[57] and was mentioned in last year's report, but now has been published. Sixty per cent of the patients had two-stage operations, and the over-all mortality was 14.8 per cent. With cancer of the head of the pancreas, only 1 has survived for three years. Three patients have survived for five years, and all had carcinoma of the ampulla. Cattell concludes that pancreatoduodenal resection should be reserved for patients with favorable lesions. With cancer of the head of the pancreas, either total pancreatectomy should be carried out or resection for this disease abandoned. On the other hand, Brunschwig[58] believes that the operation should be performed whenever a tumor in this area can be encompassed surgically. He describes a patient with cancer of the head of the pancreas who is well four and a half years after operation.

Our experience at the Massachusetts General Hospital indicates that this operation is only palliative for cancer of the head of the pancreas; if it can be accomplished easily, it should be done, but otherwise a cholecyst-enterostomy will give nearly the same prolongation of life.

Spleen and Portal Hypertension

The indications for splenectomy are discussed by Cole et al.[59] They are congenital hemolytic jaundice (with the acquired disease, results are poor in 50 per cent of cases); thrombocytopenic purpura; Banti's disease (congestive splenomegaly); thrombosis of splenic veins; Felty's disease; splenic neutropenia; primary splenic panhematocytopenia; rupture of the spleen; and cysts, primary tumors and abscesses. Spelnectomy may be advised for Gaucher's disease, ptosis of the spleen and malaria. A subcostal incision is preferred. Blakemore[60] states that when congestive splenomegaly is found, venous pressure should be taken in every case. If pressures in the gastroepiploic and coronary veins are normal and the pressures in the splenic are elevated, one can deduce that the thrombosis is in the splenic veins and splenectomy is indicated. If pressure is above 150 mm. of water in the gastroepiploic veins, a shunt operation will be necessary.

Quan and Castleman[61] found 70 normal spleens removed incidentally at other operations, such as gastrectomy, in the Massachusetts General Hospital. Eighteen patients died, and in 5 there was extensive thrombosis of the splenic and portal veins. This important paper indicates that incidental splenectomy should not be done unless absolutely necessary.

Patton and Johnston[62] have described a new tube designed to control bleeding from esophageal

varices. It is a quadruple-lumened plastic tube, with two inflatable balloons. The lower is pulled snugly up against the cardia, whereas the upper is inflated to tamponade the esophagus.

Small Intestine

Case et al.[63] have carried on an interesting series of studies on jejunal alimentation. Most of the older mixtures tended to produce cramps and diarrhea. They found that commercially prepared homogenized milk is tolerated by the jejunum from the first postoperative day. It provides 700 calories, with 38 gm. of protein, per liter. If long-term feeding is necessary, 4 per cent homogenized fat in milk (the concentration in commercial homogenized milk), enriched with protein hydrolysate up to 5 per cent and starch hydrolysate up to 6 per cent, appears to be tolerated well.

Colon and Rectum

Ulcerative Colitis

McKittrick and Moore[64] have presented an able study of the cases at the Massachusetts General Hospital from 1932 to 1947. Of 372 patients, 143 had an ileostomy, with 17.4 per cent mortality; 87 subtotal colectomy, with 8 per cent mortality; and 33 proctectomy, with a mortality of 33 per cent. Follow-up results showed that 84 per cent of survivors considered themselves in good health at the time of report.

The involvement of the ileum in chronic ulcerative colitis was determined by McCready et al.[65] from 103 cases at the Mayo Clinic. The average length of affected ileum was 20 cm., with variations from 4 to 45 cm. They believe that ileal involvement frequently causes failure of the ileostomies done for this disease.

The late care of ileostomies has been revolutionized by the Rutzen bag. The care of the ileostomy immediately after operation, so far as wound protection is concerned, is still a problem. Bellinger[66] has invented an ingenious Lucite cup that can be adjusted firmly to the skin by a rubber base with a cement. Suction may be applied, and the cup maintained for several days. This cup is also of value in any type of fistula from the abdominal wall.

Hirschsprung's Disease

Swenson and his associates[67] have presented a new theory that has changed previous concepts of the etiology of Hirschsprung's disease and initiated an entirely new method of treatment. By the use of the multiple-balloon technic it was shown that propulsive peristaltic waves are strong and present in the colon except in the rectosigmoid, where they are absent. This absence of peristaltic waves results in chronic obstruction. The malfunctioning segment is identical with the narrow, irregular bowel visualized on x-ray study. Removal of the abnormal rectum and rectosigmoid by a special modification of the pull-through operation in 34 patients has resulted in 1 death and what appears to be a complete cure in 33 patients.

Polyps

Data are gradually being collected on the incidence of rectal tumors. Ortmayer and Connelly[68] examined 1014 apparently healthy women of all ages. By barium enema, only 2 polyps were found in the entire group. By sigmoidoscopy, 1.8 per cent of the subjects demonstrated polyps. Of these 19 polyps, 1 was definitely cancer; 3 were totally benign, 8 probably benign, and 7 partly benign and partly malignant. The authors believe that these figures justify routine sigmoidoscopy in cancer-detection centers and in all thorough health surveys. X-ray study of the colon is not considered justifiable in asymptomatic subjects. In office practice where patients enter because of symptoms, the incidence of polyps will be higher. Thus, Turell[69] found adenomatous polyps in 2 per cent of the patients under forty-five years of age, whereas the incidence was 7 per cent in older patients who complained of bleeding from the rectum.

Kerr[70] investigated 100 children with polyps of the colon. Intermittent, painless passage of blood-streaked mucus was the single most common symptom. Profuse bleeding usually means that the polyp has sloughed away, as it did in 18 cases. In 68 patients a single polyp was found; 32 had more than one, and only 1 had familial polyposis. These lesions should be removed because of danger of malignant degeneration, anemia, obstruction or intussusception.

Over 50 per cent of the polyps of the large intestine can be visualized through the sigmoidoscope and should be destroyed by fulguration, according to Cattell.[71] Colotomy is required for the remainder, with a mortality of 2.6 per cent in Cattell's series. Since these patients have a higher incidence of subsequent cancer, they should be followed by x-ray examination and sigmoidoscopy.

The extensive experience of the Mayo Clinic is summarized by Buie et al.[72] in a series of 402 polypoid lesions of the rectum and sigmoid treated by fulguration. Usually, a pedunculated polyp may be fulgurated regardless of its size or position in the bowel, provided adequate exposure of the entire pedicle can be obtained. Fulguration should proceed from the tip of the polyp and only rarely from the pedicle, because of the danger of hemorrhage.

The treatment of the adenomatous polyp without a long pedicle is fraught with hazard, since the lesion may be malignant. McLanahan and his coworkers[73] have followed 31 of these patients, all having been treated by local surgical methods, and all having malignant changes in the adenoma. Twenty-eight per cent have remained well for at least a year after local removal of the polyp, whereas

10 have had recurrences, which in 5 cases were clinical cancers. The evidence indicates that microscopical demonstration of invasion of the bowel is a poor prognostic sign. A wider utilization of the principle of excision of these polyps rather than destruction by diathermy is stressed, for thereby the polyp is well treated and the pathologist has an adequate specimen.

Cancer

There is still a great deal of discussion concerning the extent of bowel that should be resected in cancer of the colon, particularly lesions of the lower sigmoid and rectum. Several investigations of fundamental pathological significance have appeared. Black and Waugh[74] studied the intramural extension of 103 cancers of the left colon. It was found that only 2 cm. of normal bowel need be allowed above and below the lesion for removal of the whole tumor. Spread of carcinoma through the bowel wall appears to follow the course of the intramural lymphatics, and the plane of greatest extension is the submucosa.

In contradiction to the study mentioned above, Connell and Rottino[75] examined 9 specimens of cancer of the rectum and lower sigmoid by serial sections surrounding the entire bowel. In 5 cases they found no retrograde spread, whereas the others had evidence of tumor 4.5 to 7 cm. below the lesion.

Evidence of venous invasion by cancer is an extremely important prognostic sign. Sunderland[76] found such invasion in 27.6 per cent of 210 cases of cancer of the rectum and sigmoid. The survival rates were 73 per cent without and 41 per cent with venous invasion in the 100 cases in which a five-year follow-up report was available.

Waugh and Kirklin[77, 78] have studied the influence of the level of the cancer of the rectum on the prognosis. Survival rates indicate that patients whose lesions lie within 5 cm. of the anal margin have a poorer prognosis, whereas those whose lesions are above 11 cm. have a better prognosis than the entire group. The location of the peritoneal reflection bears little relation to the prognosis, since the five-year survival rate with carcinoma of the rectum above the peritoneal reflection was 54.4 per cent and that of those below the peritoneal reflection was 59.4 per cent.

On the other hand, David and Gilchrist[79] found 51 per cent of patients with cancer of the rectum located below the peritoneal reflection to be free of disease in five years, compared with 65 per cent with lesions above the pelvic floor. They believe that tumor below the peritoneal reflection, because of extensive fascial and muscular attachments, as well as contiguity of other structures, made complete eradication of the cancer less certain than in high-lying tumors of the rectum. They therefore believe that the most radical operation that can be done (the Miles resection) is indicated for tumors below the peritoneal floor.

Although sphincter-saving operations are still regarded favorably by some surgeons (Bacon[80] and Best and Blair[81]), most believe that the local recurrence rate of cancer of the rectum is so high that even more radical procedures than those now in use should be carried out. Dixon[82] advises an extremely wide pelvic dissection, and Bricker[83] and Brunschwig[84] have reported probably the first cases in which a complete excision of all pelvic viscera was done in a male patient for cancer of the rectum involving the bladder.

The pendulum therefore appears to be swinging gradually back in favor of more radical operations for cancer of the rectum. We now never use a low anastomosis unless the lesion is located above the peritoneal floor and at least 5 cm. of normal bowel can be obtained beneath it, or unless the patient is incurable because of distal metastases. In this case, an anastomosis is made after excision of a cancer of the rectum, as a good palliative measure.

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Correction. In the concluding section of the Medical Progress Report by Dr. John Godwin Downing entitled "Dermatologic Therapy," which appeared in the April 13 issue of the *Journal*, the last sentence in the first paragraph on page 585 should be changed to read "I have been using dl-alpha-tocopheryl acetate (ephynal acetate) in chronic discoid lupus erythematosus with varying success."

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 36271

PRESENTATION OF CASE

First admission. A thirty-seven-year-old housewife was admitted to the hospital for repair of a cystocele and lacerated cervix. She had had seven pregnancies, which were followed by normal lactation. Severe hemorrhage followed a dilatation and curettage and routine plastic repair, and six days after the plastic repair the cervix was amputated. The patient was discharged in good condition on the twenty-fifth hospital day.

Second admission (twenty years later). The patient had a spontaneous normal menopause at the age of forty-five. She had always had a somewhat withdrawn personality, but at about the age of fifty-four she began to spend most of her time in her room. She complained of fatigue and weakness and developed a craving for sweets. For seven weeks before her second admission, she was too weak to do any housework or shopping. Two weeks before admission a series of dental extractions was begun. For six days before entry she refused all food and took only minimal amounts of water. On the morning of admission she was cold, sweaty and totally unresponsive.

Physical examination showed a semicomatose woman with a pulse of 80 and a blood pressure of 120 systolic, 80 diastolic. The lungs were clear, and the abdomen soft without masses. The axillary hair was absent, and the pubic hair was scanty and of female distribution. The skin was pale, and the face expressionless. No abnormal pigmentation was seen. Knee and ankle jerks were absent. The blood sugar was 50 mg. per 100 cc. The patient became active and oriented immediately after an infusion of 10 per cent dextrose in saline solution.

Urine obtained after this infusion had a specific gravity of 1.018, with occasional red and white cells in the sediment. There were a + test for albumin, a red sugar reaction and a ++ test for acetone. Examination of the blood showed a red-cell count of 3,680,000, with 10.5 gm. per 100 cc. of hemoglobin, and a white-cell count of 11,400, with 91 per cent neutrophils. The nonprotein nitrogen was 19 mg., the protein 5.3 gm., and the cholesterol 236 mg. per 100 cc., and the chloride 92 milliequiv., the sodium 117 milliequiv., and the potassium 4.45 milliequiv. per liter. Corticosteroid excretion was 0.04 mg. in twenty-four hours. No 17-ketosteroids were detectable. Follicle-stimulating hormone (FSH) excretion was positive for 52 mouse units in twenty-four hours. Films of the skull were normal. X-ray examination of the chest showed a small heart and some calcification in the left hilar region and mediastinum. Plain films of the abdomen were negative. The basal metabolic rate was –8 per cent on one determination. An electrocardiogram showed a normal rhythm of 35, very small QRS waves in the limb leads, very low T waves in Lead 1 with slight late dip, inverted T waves in Leads 2 and 3 and a prolonged systole measured by a QT interval of about 0.45 second.

The patient responded well to intravenous fluids and electrolytes, desoxycorticosterone acetate (DOCA), adrenocortical extract and testosterone. She was discharged after twenty-six days of hospitalization on a regime of DOCA, thyroid and added salt.

Third admission (three and a half years later). In the course of the next three years several minor crises were precipitated by upper respiratory infections, gastrointestinal upsets and an abscessed tooth, but all were treated successfully at home with increased amounts of DOCA and saline solution. During this period the patient developed progressive contracture of both knee joints. This admission was preceded by a brief period of confusion and one bout of vomiting after which she went into stupor. Physical examination showed a restless, disoriented woman with a hacking cough and a temperature of 103.6°F. The systolic blood pressure was 85, and the diastolic was not obtainable. The lungs were clear, and the abdomen soft. Urinalysis was negative except for a few red cells and casts in the sediment. Examination of the blood revealed a hemoglobin of 12.5 gm. and a white-cell count of 12,500, with 80 per cent neutrophils. The sodium on admission was 136.2 milliequiv., the potassium 4.6 milliequiv., and the chloride 103 milliequiv. per liter, and the sugar 109 mg., the nonprotein nitrogen 25 mg., and the cholesterol 174 mg. per 100 cc. Urine culture was negative. FSH excretion was positive for 13 mouse units in twenty-four hours. X-ray examination of the chest showed a density in the right middle lobe consistent with an infarct. Films of the pelvis disclosed degenerative

changes about the right hip joint and around the symphysis pubis. The patient responded satisfactorily to penicillin, intravenous administration of dextrose in saline solution, DOCA and lipoadrenal and aqueous adrenocortical extract and was discharged after nine days on DOCA, methyl testosterone and sodium chloride.

Fourth admission (seven months later). The patient did moderately well until two days prior to admission, when she developed coryza followed by drowsiness, vagueness, thirst, anorexia and vomiting. Physical examination revealed a temperature of 98.6°F., a pulse of 88, respirations of 20 and a blood pressure of 98 systolic, 60 diastolic. There was a hacking cough productive of thick, white sputum, but the examination was otherwise negative. The blood sugar was 69 mg. per 100 cc., and the sodium 126 milliequiv., and the potassium 4.7 milliequiv. per liter. An electrocardiogram showed essentially the same pattern as the previous tracings except that the QT interval had decreased to 0.34 second. The patient was given Crysticillin and the usual hormone therapy and was discharged improved on the seventh hospital day on increased dosage of DOCA and additional salt.

Final admission (two and a half months later). She did well until two weeks before the final admission, when she became drowsy and appeared to have deteriorated mentally. The blood pressure at this time was 90 systolic, 70 diastolic, and the sodium 127 milliequiv. per liter. She was thought to have been swallowing her DOCA tablets instead of taking them sublingually. She improved on intramuscular medication and increased salt (6.0 gm. a day for four days). She then developed edema, and salt and DOCA were omitted for three days. Six days before admission she had many visitors and complained of fatigue. On the following day she had an episode of fainting relieved by 10 cc. of 50 per cent glucose intravenously. The blood pressure was 120 systolic, 80 diastolic, and no DOCA was given, since edema persisted. Two days before admission the blood sugar was 52 mg. per 100 cc., and the serum sodium 117 milliequiv. per liter. On the following day she refused food and was given 500 cc. of 10 per cent dextrose in saline solution intravenously and 2 mg. of DOCA, and was placed on 1 cc. of lipoadrenal extract every eight hours. She improved, and ate well the rest of the day. On the morning of admission she vomited and was very drowsy.

Physical examination revealed a semicomatose woman with a temperature of 99.1°F., a pulse of 72 and respirations of 20. The blood pressure was 92 systolic, 60 diastolic. The right pupil was larger than the left, all extremities were somewhat spastic, abdominal reflexes, knee jerks and ankle jerks were absent, and there were bilateral Babinski reflexes.

The urine had a specific gravity of 1.026 and gave a ++ test for albumin, a mustard-colored sugar reaction and a +++ test for acetone. The blood sugar was 121 mg., and the total protein 5.0 gm. per 100 cc., and the sodium 111 milliequiv., the potassium 4.2 milliequiv., and the chloride 82 milliequiv. per liter. The nonprotein nitrogen was 11 mg., and the blood urea nitrogen 3.8 mg. per 100 cc. (both these values were checked). An electrocardiogram showed a rate of 80 with a PR interval of 0.18 second. There was low voltage in all complexes of Lead 1 and of the QRS complexes throughout. The QT interval was 0.46 second. The T waves were upright in Leads AVR and AVL, flat in Leads 1 and V_6, upright to inverted in Lead V_3 and inverted in Leads 2, 3, AVF, V_4 and V_5, with low voltages in all Leads except V_6.

In the twenty-two hours of the hospital course the patient received 2000 cc. of 10 per cent dextrose in saline solution, 300 cc. of physiologic saline solution and 700 cc. of 5 per cent dextrose in water, all intravenously, 140 cc. of aqueous adrenocortical extract intravenously and 10 cc. intramuscularly and 300,000 units of penicillin. The urinary output during this period was 575 cc. On the evening of the first hospital day occasional ventricular premature beats were heard and moderate Cheyne–Stokes breathing began. Soon runs of 8 to 16 rapid beats appeared, and multifocal ventricular tachycardia was demonstrated by electrocardiogram. During the episodes of tachycardia the respirations became deep and stertorous, the eyes rolled up, and the patient became rigid without convulsive movements. Quinidine lactate, 0.05 gm., was given cautiously intramuscularly. The patient remained comatose throughout the night and the blood pressure ranged around 100 systolic, 60 diastolic. Twenty-one hours after admission she stopped breathing, and no heart sounds, pulse or blood pressure could be obtained. Then grunting respirations were noted at intervals of about forty seconds. One cubic centimeter of intracardiac epinephrine produced no change, and oxygen and artificial respiration were started. Electrocardiograms showed absent P waves and bizarre QRS complexes of 0.14 second's duration occurring irregularly with periods of asystole lasting up to 10 seconds and runs of ventricular tachycardia at 165 seconds. A mixture of Coramine with caffeine sodium benzoate was given intracutaneously followed by 0.5 cc. of 20 per cent potassium chloride intracutaneously without improvement. Later 1 cc. of 20 per cent potassium chloride was given by vein, also without improvement. About forty-five minutes after the episode started the electrocardiogram showed only a few bizarre ventricular complexes, and then no evidence of heart action. The patient became cyanotic, and was pronounced dead.

Differential Diagnosis

Dr. J. H. Means*: This is the case of a woman with a chronic malady, which I am sure was mainly one of insufficiency of the adrenal cortex and was characterized by a series of episodes that seemed to be fairly classic Addisonian crises and finally a fatal one. The problem, as I see it, is not whether she had adrenocortical insufficiency but rather what kind it was, whether it was primary or secondary, what it was due to and what else if anything she had.

I shall comment on certain items in the record first. At the age of fifty-four, seventeen years after the first admission, the patient apparently had a personality change. She developed a craving for sweets, which I suppose may have been a symptom of hypoglycemia. About two weeks before the second admission, she had a series of dental extractions, which in any patient who has insufficient adrenocortical function might precipitate a crisis. On the morning of that admission she had an episode similar to the crises seen in patients who have proved adrenal insufficiency. At that time there was a slight leukocytosis. The fact that the urine contained sugar may have been connected with the infusion of dextrose; I cannot explain the acetone. The low corticosteroid secretion and absence of 17-ketosteroids were both strongly in favor of practically no adrenocortical function. FSH excretion was suggestively high; electrocardiographic findings were similar to those seen in hypothyroidism or hypoadrenal function. There was a small heart, which is a characteristic finding in Addison's disease. The normal blood pressure is a little troublesome from the point of view of my theory.

At the third admission the FSH was 13 mouse units in twenty-four hours, which Dr. Albright tells me is not low. That is very important. There was x-ray evidence of a pulmonary infarct, but nothing in the history suggesting the legs as a source, although they are often involved.

Could we see the x-ray films?

Dr. Stanley M. Wyman: These are the original films, showing clear lungs; the heart shadow appears to be well within normal limits.

Dr. Means: You mean it is not larger than normal. Do you think it is smaller than normal?

Dr. Wyman: I am very hesitant to say that.

Dr. Means: What about the sella turcica?

Dr. Wyman: The sella turcica seems normal; the clinoid processes show no erosion, and there are no abnormal calcifications in the region. On films taken a few days after the original chest films, the heart appears a little larger. A shadow in the right lung is seen overlying the right hilus and appears to lie well forward in the chest. It is perfectly consistent with an infarct or with atelectasis. There is no evidence of calcification above the kidneys in the region of the adrenal glands.

I do not think there is anything of importance about the degenerative changes reported in the hip joints and symphysis other than those we commonly encounter.

Dr. Means: Thank you very much. I might just point out in my defense that some other radiologist must have called this a small heart. Just to stick my neck out a little farther, I am going to guess that the heart weighed less than normal.

During the last admission the patient had albuminuria, but I do not believe she had any important renal lesion. Tests for sugar and acetone were positive in the urine, and the blood sugar was somewhat high so that one wonders if she might have become somewhat diabetic. There were bizarre electrocardiographic changes, and I should like to have an electrocardiographer tell us what light these changes throw on the electrolyte situation. The potassium was not low at any time.

Dr. James H. Currens: The electrocardiogram during the last admission was very bizarre. It was my impression that it was consistent with but not necessarily diagnostic of a deficiency of intracellular potassium. The electrical systole as manifested by the QT interval was prolonged, and there was significant depression of the RST segments as well as the T waves. The QRS interval was also increased. I should like to point out the fact that somewhat similar changes in the electrocardiogram have been noted in rats dying as a result of potassium deficiency — that is, in animals maintained on a potassium-deficient diet. The normal serum potassium is not necessarily disturbing since correlation between electrocardiographic changes and serum potassium levels is nil at times.

Dr. Means: I shall say this much for my diagnosis, that the chief factor was adrenocortical insufficiency and the chief differential diagnosis, it seems to me, is between Addison's disease and Simmonds's disease or its subspecies, Sheehan's disease. One wonders about the significance of that hemorrhage after dilatation and curettage. Sheehan's disease is found in women who have severe postpartum hemorrhage followed by infarction of the pituitary body and panhypopituitarism. This patient did not have a post-partum hemorrhage but a hemorrhage from the uterus after a dilatation and curettage. Sheehan,[1] in his paper, makes no mention of this type of syndrome developing after any hemorrhage other than post-partum hemorrhage. Several years later the patient had a perfectly normal menopause, which practically rules out Simmonds's syndrome. However, to my way of thinking, the absence of pigmentation favors a diagnosis of adrenocortical insufficiency secondary to pituitary failure. In primary Addison's disease pigmentation occurs in over 95 per cent of the cases, and there is probably a higher incidence in fatal

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cases. Of course there are panhypopituitarisms other than Simmonds's disease, such as those caused by a tumor impinging on the pituitary body or any of the other things that may destroy the pituitary body or reduce its function. Since there is no evidence of a pituitary lesion, however, I am very skeptical about a primary pituitary source for this syndrome.

There was only one determination of the basal metabolic rate, which was −8 per cent. Dr. George Thorn tells me that in most cases of classic Addison's disease, the basal metabolic rate is around −20 per cent. One would expect an even lower rate in Simmonds's disease. Of course, one test is not very important.

The normal to high FSH, it seems to me, practically excludes hypofunction of the pituitary body; therefore, I am forced to say that this was primary Addison's disease and I do not know why there was no pigmentation. If it was primary Addison's disease, which kind was it? Was it primary atrophy or tuberculosis of the adrenal glands? I do not believe there is very much in the record to suggest tuberculosis, — the x-ray films do not show any, — so that I would favor the atrophic variety of Addison's disease.

Now the question arises, Were there any other endocrinopathies here? I just do not know about the thyroid gland. Thyroid was given to the patient so she was considered to have been mildly hypothyroid. There is nothing that I can see that would justify my saying that she had any hypothyroidism. Toward the end there was a little flock of items that suggested that she might be getting diabetic but I cannot really say that she was. I think that Dr. Mallory found atrophic to absent adrenal glands, a normal pituitary body and probably a normal thyroid gland. I cannot say that he found anything else except a small heart. I think that is as far as I can go.

Dr. Reed Harwood: I would like to add to the information in the record that she did look like a patient with myxedema.

Dr. Means: Why should she have had myxedema with Addison's disease? She should not. She may very well have had myxedema with Simmonds's disease, of course. Yet I cannot for the life of me see how she could have had Simmonds's disease with this normal menstrual story, normal menopause and the normal to elevated FSH secretion. It just does not make sense as far as my meager knowledge goes.

Dr. Harwood: I would like to point out that the patient went four years without any hypoglycemia, and then it gave her quite a little trouble during the last month of her life. I should like to ask Dr. Albright why it was that she could be brought out of her crises for a long time and then suddenly did not respond at all.

Dr. Means: There might have been some infection, I suppose, that made her more resistant to treatment.

Dr. Fuller Albright: I cannot answer Dr. Harwood's question. This patient belongs to a group of about 5 patients we have seen in whom there were all the symptoms and findings of panhypopituitarism except that the FSH was normal. We rather think that the hormones of the pituitary body except the FSH come from the eosinophil cells. We believe that in these cases there is a lack of eosinophil cells and normal basophils. This is the first autopsy that we have had in any of this group, and we are very anxious to see if the eosinophils have all disappeared.

Dr. Jacob Lerman: I would like to ask Dr. Means if he places any emphasis on the drop in FSH of 52 to 13 mouse units? Does that perchance mean a progressive destruction of the pituitary body? The first one mentioned was 52 mouse units. We assume that the highest positive dilution is recorded.

Dr. Albright: There is no evidence that there was a drop in the FSH titer. The first test was "positive for 52 mouse units per day," and the second was "positive for 13 mouse units per day." The second test was not assayed for 52 mouse units and might have been positive at this level.

Dr. Harwood: I understand myself that the FSH was not quite as strongly positive on the second determination.

Dr. Albright: I did not say that the FSH test was not high; it was not low for the normal mature woman. It may have been low for the postmenopausal woman.

Dr. Means: I am placing a great deal of weight on the FSH. If there is something phony about that, my argument falls to the ground.

Dr. Andries Querido: If this patient really was myxedematous, with Addison's disease, I think one would have to consider biglandular disease with a normal pituitary body. The one such case I have seen was strongly pigmented. I think that the absence of pigmentation may be an argument against a normal pituitary body in this case.

Dr. Frederic C. Bartter: I wonder if possibly some of the difference was due to the fact that she was not hypothyroid during the entire time but only during the last few months.

Dr. Lerman: Falta[2] has described patients with biglandular disturbance, Addison's disease and myxedema, but in those cases I think, as Dr. Querido said, there was pigmentation.

Clinical Diagnoses

Panhypopituitarism.
Addison's crises.

Dr. Means's Diagnosis

Addison's disease, atrophic type.

Anatomical Diagnoses

Atrophy of anterior lobe of pituitary body, severe, with hypopituitarism.
Atrophy of thyroid gland and adrenal cortex, secondary.
Alopecia, axillary.
Pulmonary tuberculosis, apical, bilateral, healed.

Pathological Discussion

Dr. Tracy B. Mallory: Autopsy on this patient showed atrophy of three endocrine organs — the pituitary, the thyroid and the adrenal glands. The pituitary body showed a minute crescent of anterior lobe, perhaps 10 per cent of normal volume, surrounding an apparently normal-sized posterior lobe. Sections of the pituitary gland at autopsy are often very difficult to interpret because of postmortem changes. I thought both eosinophils and basophils were markedly decreased and that the chromophobes made up the bulk of the persisting glandular tissue. Material was sent to Dr. A. E. Severinghaus, of New York City, because of his expert knowledge of pituitary cytology. He agreed that the eosinophils were markedly decreased but believed that there was only a slight reduction in the number of basophils. I have no doubt he is correct, and therefore Dr. Albright can consider his hypothesis vindicated.

The thyroid gland weighed only 5 gm. and showed extensive atrophy and fibrosis and comparatively little inflammation. The two adrenal glands together weighed 5 gm. and were almost paper thin. The medulla was relatively well preserved. The cortex showed very marked atrophy, with almost complete lipoid depletion. There was also extensive fibrosis in the adrenal glands but no evidence of any inflammatory process. In the lungs small scars of old tuberculosis were found at the apexes but nothing active, and there was one fibrotic lesion that was consistent with a healed infarction. The heart was small, weighing 260 gm. That is not extremely small, however, for a small woman.

Dr. Means: It was, however, somewhat small. What was the weight of the pancreas?

Dr. Mallory: The pancreas weighed 60 gm., which is considerably less than normal, but microscopically was not very striking in appearance. One hyalinized island of Langerhans was found. The majority of the islands looked quite normal. There was no fibrosis or fat infiltration.

Dr. Querido: The interesting point here is the question of the etiology of this disease. If one has to stick to the definition of Sheehan, the patient should not have had anterior-lobe insufficiency. It might be that this case was similar to those described by Falta[2] that have occasionally appeared in the literature. She may have had a multiglandular fibrosis, and the hemorrhage had nothing to do with it. This would be the first case as far as I know studied with modern endocrinologic methods.

Dr. Mallory: One of the difficulties with accepting severe hemorrhage and shock-like states as the etiology of hypopituitarism is the very marked predilection of the disease for females, whereas males suffering traumatic injury — battle casualties, for instance — suffer as profound states of shock as any pregnant female ever suffered, and yet a pituitary insufficiency rarely, if ever, develops. So far as the Falta syndrome is concerned, it assumes a simultaneous sclerosis of several endocrine glands. His cases were studied only clinically without confirmatory anatomic checks, and therefore his theory is only an unproved hypothesis.

References

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CASE 36272

Presentation of Case

A seventy-four-year-old newspaper editor was admitted to the hospital because of back pain.

Three months prior to admission the patient had an episode of cough, chest pain and malaise diagnosed as virus pneumonia. Following recovery from the acute symptoms he continued to feel rather poorly for several weeks. A chest x-ray film taken by a health-department mobile unit four months before admission was reported as normal. Advancing phimosis had troubled the patient, and two months before entry his physician advised circumcision. Five weeks before admission, while shoveling snow, he developed sudden severe pain in the thoracic spine, especially on the right side, and sharp pain in the chest. The pain persisted and crippled him increasingly so that finally he was unable to walk. He complained of increasing constipation, with questionable "dark-blue" stools, and claimed about 10 pounds of weight loss recently.

Physical examination showed a pale, poorly nourished, tremulous man, with slow, hesitant speech, who appeared to have been old longer than the history indicated. There was slight thoracic scoliosis, a marked barrel chest and tenderness over the upper thoracic vertebras. He was unable to sit erect because of back pain. Severe phimosis was present. The prostate was slightly enlarged and soft.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 85 diastolic.

Examination of the blood revealed 11.2 gm. of hemoglobin and a white-cell count of 5600, with 82 per cent neutrophils. Urinalysis disclosed a specific gravity of 1.020 and a +++ test for al-

bumin. The serum nonprotein nitrogen was 26 mg., the calcium 10.9 mg., and the phosphorus 2.7 mg. per 100 cc., and the phosphatase 1.6 units per 100 cc. A stool specimen was guaiac negative. A blood Hinton test was negative. X-ray films of the dorsal spine revealed extensive demineralization of all the bones of the spine, with wedging of the bodies of the eighth and eleventh dorsal vertebras. The joint spaces were preserved. The bones of the lumbar spine and pelvis showed diffuse demineralization, with a localized area of rarefaction in the right second and third sacral segments.

Following admission a circumcision was planned because of the marked phimosis. However, during the first few days his condition rapidly deteriorated, with a maximum temperature of 102°F., disorientation, distention of the bladder and some apparent stiffness of the neck. A lumbar puncture revealed a spinal fluid under an initial pressure equivalent to 140 mm. of water, a total protein of 49 mg. per 100 cc. and a sugar of 138 mg. per 100 cc. The gold-sol curve was 0001222211. A dorsal slit of the prepuce was done, a Foley catheter was inserted, and a few days later a circumcision was performed. The patient continued to run a temperature from 100 to 102°F. and seemed drowsy though he continued to respond to direct commands and simple questions. He was seen by a neurologic consultant, who found tendon reflexes in the arms equal, the right knee jerk greater than the left and the left ankle jerk absent. The plantar reflexes were both extensor. X-ray films of the skull showed extensive demineralization of the bones. The pineal gland was insufficiently calcified for localization. There were no localized areas of bone destruction. The sella turcica was of average size and smooth in contour. A chest film revealed an irregular patchy density in both lung fields. There was also a suggestion of some fluid in the right costophrenic sinus. The heart was transverse in position. There was marked sclerosis and tortuosity of the aorta. Blood culture produced no growth; a catheterized urine specimen showed only rare colon bacilli. About ten days following admission the serum calcium was reported as 12.6 mg., the phosphorus 3.7 mg., and the nonprotein nitrogen 68 mg. per 100 cc. The patient continued to fail slowly and died quietly about three weeks after admission.

Differential Diagnosis

Dr. Reed Harwood*: In summary, this seventy-four-year-old man suffered fractures of the spine while shoveling snow, and had increasingly severe pain, which forced him to bed and finally into the hospital. He was found to have generalized demineralization of the skeleton, a high serum calcium, albuminuria and anemia. He developed a fever, a questionable pulmonary lesion and nitrogen retention, and he died eight weeks after the snowstorm.

May we see the x-ray films?

Dr. Stanley M. Wyman: The first examination of the spine shows rather pronounced collapse of one of the midthoracic and another lower thoracic vertebral bodies. There is generalized demineralization, as noted in the record. The area of rarefaction in the sacrum, although suggestive of bone destruction, can be due to an overlying loop of bowel. The films of the skull show no very striking demineralization. However, there are one or two small round areas of radiolucence, which make one wonder about localized bone destruction. These films of the chest taken with a portable machine are not very satisfactory, particularly the lateral view, but they show patchy density in both lung fields. I do not think I would want to go much farther in describing it.

Dr. Harwood: Was the film of the chest taken on admission?

Dr. Wyman: Four days after that. There are radiolucencies in the left clavicle, also suggestive of localized bone destruction.

Dr. Harwood: How about the ribs?

Dr. Wyman: The films are not ideal for showing rib detail.

Dr. Harwood: I got the impression from the protocol that there was a good deal more demineralization, particularly in the skull, which was said to show extensive demineralization.

Dr. Wyman: I think the skull is not too demineralized, but I do think there may be some patches of rarefaction in it.

Dr. Harwood: Would you say that the chest film suggests infection, tumor infiltration or edema?

Dr. Wyman: I do not think it looks like edema. It might be a patchy pneumonitis. One certainly has to bear in mind the possibility of lymphatic spread of metastases. The bony changes suggest widespread bone-marrow involvement.

Dr. Harwood: Let us turn to the record and discuss a few points that are brought out in the history. First, it states the patient had virus pneumonia. I have no reason for not accepting that diagnosis although it is possible that it was the first manifestation of widespread metastatic disease of the lung. Then constipation is mentioned. It is possible that the constipation was due to inactivity or possibly to a neurogenic disturbance from spinal-cord compression following the fractures. I will keep in mind the possibility of carcinoma of the stomach or bowel to explain the constipation. The urine specimen had a normal specific gravity, and there was a normal nonprotein nitrogen, so that I believe the patient had no serious renal disease at the time of admission. I do not know how to interpret the terminal rise in nonprotein nitrogen. It may have been simple dehydration, or it may be that the kidneys became involved in the patho-

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logic process during the last three weeks of life. I will discuss that later.

Another thing mentioned in the protocol is the distention of the bladder. This could have been due to moderate prostatic hypertrophy in an elderly man who was put to bed or to a neurogenic bladder following spinal-cord compression. The positive Babinski sign makes me think that the patient did have some compression of the spinal cord although in a man of this age it is possible to find positive Babinski signs from senile degeneration of the brain. The elevated spinal-fluid sugar, if the patient had not received an intravenous glucose injection before the lumbar puncture, suggests that he had diabetes. That makes one wonder if the marked albuminuria might not have been due to intercapillary glomerulosclerosis.

Now I come to a discussion of the various causes of demineralization. The first is senile osteoporosis. Some degree of osteoporosis is present in all old people but is especially likely to be seen in women. In this condition the spine and pelvis are most often involved, and the long bones are involved in severe cases. The skull is almost never involved. Osteoporosis rarely causes spinal-cord compression. Dr. Wyman, did you say that he had no demineralization of the skull?

DR. WYMAN: Certainly nothing that strikes me as being very prominent.

DR. HARWOOD: May I ask if that is consistent with senile osteoporosis?

DR. WYMAN: That is certainly what one would see in senile osteoporosis. I would not expect to see the areas of localized rarefaction, however.

DR. HARWOOD: It is very likely that this man had some senile osteoporosis, but, as Dr. Wyman pointed out, there are some suspicious changes that suggest some other diagnosis.

The second cause of dimineralization is osteomalacia, which is due to a deficiency of intake of minerals, fats and vitamin D, or a deficiency in the absorption of these things, such as is seen in cases of steatorrhea. I think the history satisfactorily excludes this possibility. The third cause is renal rickets. Usually, in this condition there is a long history of renal disease preceding the bone disease. The demineralization of bone is generally accompanied by metastatic calcium deposition, particularly in the arteries and in the neighborhood of the joints. The serum calcium is usually low, and the phosphatase is high.

The fourth cause is hyperparathyroidism. The evidence for hyperparathyroidism in this case is as follows: the patient had two serum calciums, one just above normal and the second quite definitely high, and two determinations for serum phosphorus, the first being low, and the second, accompanied by evidence of renal failure (in which the phosphorus would be expected to rise), being normal. He had a normal alkaline phosphastase, but with the amount of bone disease present the phosphatase would almost certainly be high if he had hyperparathyroidism. I am inclined to think that hyperparathyroidism will have to be excluded completely.

The fifth cause is multiple myeloma, which may simulate the osteoporotic type of hyperparathyroidism, radiologically, chemically and clinically. The demineralization in multiple myeloma is rarely quite so generalized as is seen in hyperparathyroidism, and the serum phosphorus is rarely abnormal. The phosphatase is usually normal.

The sixth cause is metastatic cancer, which may produce a similar x-ray picture and occasionally a high serum calcium with or without a high phosphatase.

The seventh and eighth causes are hyperthyroidism and Cushing's syndrome. Both can be excluded without further comment.

Let us look for a moment at the conditions that produce hypercalcemia, leaving out such obviously inappropriate conditions as overdoses of vitamin D or of AT-10, leukemia and polycythemia. The first is hyperparathyroidism, in which the phosphatase is elevated. The second is myeloma, which causes a high serum calcium in association with a high serum protein, but a normal or slightly increased phosphorus and a normal phosphatase. If I am going to end with a diagnosis of multiple myeloma, I am going to do so without the benefit of certain important laboratory findings — namely, an elevated serum protein, the presence of Bence-Jones protein in the urine and the finding of plasma cells in the blood smear. The third condition is skeletal metastases, in which the calcium is usually normal but is occasionally high, the phosphorus normal and the phosphatase normal or increased. The fourth is acute bone atrophy, as in immobilization with a fracture or paralysis. The calcium in such cases may be high for a while, and the

phosphorus and phosphatase are normal. I do not think we can include this in our diagnosis because the thing that put the patient to bed was the fracture. The fifth condition, advanced nephritis, rarely shows a high calcium, more often a low calcium and a high phosphorus.

It seems to me that the choice is narrowed to one between metastatic disease and multiple myeloma. The diagnosis I prefer is multiple myeloma. This condition can produce severe demineralization, fractures, albuminuria, renal failure and anemia, all of which were present in this case. It also causes hypercalcemia with a normal phosphatase in about two thirds of the cases. I am making multiple myeloma my first diagnosis and metastatic carcinoma, with the site of the original focus undetermined, as my second guess.

Dr. Tracy B. Mallory: Dr. Chapman, I believe you saw this patient in the hospital.

Dr. Earle M. Chapman: I admire Dr. Harwood's review of the situation because he brought up a diagnosis that I did not seriously consider, nor did the consultants. I had been misled into thinking that the situation was primarily pulmonary and that the patient probably had metastatic disease. The patient came into the hospital looking much worse than is apparent from the protocol. He came in on a Friday, and on Saturday night sedation was ordered for him and he received in error more medication than was probably good for him. By Monday morning there had been a pronounced change in his whole behavior — confusion and fever — that I first attributed to overmedication. I stopped all drugs and gave the patient intravenous injections of glucose in saline solution and in distilled water, but to my surprise he did not respond to the treatment so that then I began to think that the medication was a red herring.

Then, of course, there was the phimosis. Here was a man with the tightest foreskin that I have ever seen. The nurses reported that the patient had urinated, but the bed was always dry when I saw it and I did not think he could excrete any urine. The genitourinary consultants who saw him thought that the foreskin would eventually shut down entirely, and a dorsal slit was done. The lumbar puncture did not help us; it only confused us. We were seeking evidence of a cord bladder, but we did not think there could be a block with a total protein of only 49 gm. per 100 cc. I do not know what else we could have done for him, but we certainly were laboring under diagnostic errors.

Dr. Jacob Lerman: Diffuse lymphoma of the bone would give a similar picture to multiple myeloma.

Clinical Diagnosis

? Carcinoma of lung, with metastases to brain and thoracic vertebras.

Dr. Harwood's Diagnosis

Multiple myeloma.

Anatomical Diagnoses

Multiple myeloma.
Nephrosclerosis.
Arteriosclerosis, generalized.
Pulmonary edema.
Bronchopneumonia.

Pathological Discussion

Dr. Mallory: Autopsy showed very little of significance in the viscera. The heart and liver were slightly atrophied, like those of an old man. The kidneys were small and scarred as is seen with arteriosclerosis, which was quite severe. There was also severe sclerosis in the abdominal aorta. When we came to examine the spine, a tumor was found in the region of the fourth and fifth thoracic vertebras lying in the spinal canal, infiltrating rather diffusely the epidural fat but not penetrating the dura and compressing the spinal cord only very slightly. The epidural tumor was continuous with a rarefied lesion in the vertebra and also with a tumor that extended outward from the vertebra along the intercostal space for a considerable distance alongside the spine. Microscopical examination showed that this tumor was composed entirely of well defined plasma cells, and there is no doubt that plasma-cell myeloma is the final diagnosis. There was no evidence of a myeloma kidney, which is often seen with this condition but usually with the association of Bence–Jones protein in the urine. The renal lesion was purely vascular and the result of arteriosclerosis.

Dr. F. Dennette Adams: Did the lungs show any lesion?

Dr. Mallory: The lungs showed a slight patchy edema and a little pneumonia.

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Formerly

The Boston Medical and Surgical Journal

Established 1828

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MATERIAL, other than original articles, should be received not later than noon on Thursday, three weeks before date of publication.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

REORGANIZATION PLAN 27

NEARLY a year ago federal Reorganization Plan 1, introduced by the President, was finally defeated in the Senate. Plan 1, which was based on the creation of a department of welfare under a secretary with cabinet status, was defeated because of the undesirable grouping in it of agencies that did not naturally belong together, and the subordination of the nation's health to the status of the other interests.

Last year's executive plan to create a department of welfare has become this year's Plan 27 to create a department of health, education and security, with each of its divisions featured in the title, but still consisting of an illogical tripartite alliance of convenience. Each division in this new department would have its own head — a surgeon general of the Public Health Service, to represent the nation's health; a commissioner of education and a commissioner of social security. Each of these heads would report directly to the Secretary of Health, Education and Security, but their possible relation to the Under Secretary of Health, Education and Security, the Assistant Secretary of Health, Education and Security, and the Administrative Secretary of Health, Education and Security are not so clearly defined. The above-listed secretaries, however, would perform such duties as the Secretary might prescribe; the Surgeon General, the Commissioner of Education and the Commissioner of Social Security are listed simply as "other officers."

None of these officials need be physicians, not even, apparently, the new surgeon general, who *may* be appointed from the Commissioned Regular Corps of the Public Health Service, but is not required to be.

The American Medical Association, representing the great majority of the physicians of the country, and many other thoughtful persons, including, it is to be expected, a majority of the Congress, still believe that the nation's health deserves a separate department in the Government, under the direction of a qualified physician.

To defeat Plan 27 this year, either the House or Senate must vote to support a resolution of opposition prior to July 31.

The message of the President transmitting Government Reorganization Plan 27 of 1950 to the Congress announces that the present plan has been substantially modified to meet the criticisms directed against Plan 1 of 1949, at the same time stating the belief that the criticisms of Plan 1 were not well founded. It is further specifically stated that the Secretary of Health, Education and Social Security would be vested with essentially the same duties and authority as are now vested in the Federal Security Administrator. These specifications will hardly endear the plan to a number of observers or create in them a feeling of complete confidence.

Two main objections have been raised to Plan 27. The first is the subordination of health, which, according to the program of the American Medical Association, should have a separate department

of cabinet status, with a secretary who is a doctor of medicine. The second relates to the lack of qualifications of the new secretary as proposed, and is based on the fear that he might be one who neither understands nor is sympathetic with the problems, the goals and the ideals of medical practice and public health. Of all cabinet positions, that of health should be vested in a person who not only understands its problems, but can set himself to their solution relatively unhampered by personal ambition.

It may be feared that while the voice is that of Jacob, the hands may still be those of Esau.

CARE-UNESCO BOOK FUND PROGRAM

CARE, an abbreviation of Cooperative for American Remittances to Europe, Inc., for those who are alphabetically absent-minded, has released a report on its "Food for the Mind" program, initiated last year. At that time, as mentioned in these columns on September 29, 1949, announcement was made of the tremendous loss of books suffered by many European universities and medical schools, and a plan for replacements from this country was outlined.

CARE now announces that medical books are in greater demand than those of any other of the twelve categories made originally available through the CARE-UNESCO Book Fund Program. Medical volumes, in line with the requests that have been constantly received, have already been included for most of the institutions reached in the original deliveries of some $50,000 worth of books.

The literary deficit of Europe needs no explanation, with a wartime blackout of research added to wartime confiscations and destruction of books. To this is now added the lack of dollar credit with which to buy the books so easily available in America.

Lists of book needs are received from foreign institutions and are filled as closely as possible by purchases of the latest and best books in the English language. These purchases are based on a bibliography of 1600 titles compiled by a special book committee of acknowledged experts; they are covered at the publishers' list prices through special publishers' discounts and ECA ocean-freight subsidies. Countries presently being reached include Austria, Belgium, Czechoslovakia, Finland, France, Great Britain, Western Germany and Berlin, Greece, Italy, Norway, the Netherlands, Malta, Japan, Korea, the Philippines, Pakistan and Siam.

Donors to the Book Fund Program are invited to send only money and leave the rest to CARE—an appeal that has the endorsement of the Council of the Massachusetts Medical Society which, at its annual meeting in May, adopted the recommendation of its Committee on Medical Education to this effect.

APPRENTICE SYSTEM AT YALE

SEVEN Yale medical students, as part of a recently established project, devoted a week last May to serving as voluntary apprentices to various Connecticut general practitioners. One student went to Willimantic, and the others in pairs to Torrington, where they lived in quarters provided by the local hospital and were by day assigned to their preceptors.

The art being long, even a week of such elective duty is all too short in which to see deeply into the problems of the general practitioner. It may be hoped that what these young men observed, however, was such as to kindle in them a desire to cultivate the personal relations of medicine rather than to discourage them from this pursuit.

With two thirds of the nation's physicians engaged in general practice of varying scope this diversified specialty all the more requires an exacting training and deserves a sympathetic respect. The art of practice cannot be taught at all in medical schools and hardly in hospitals. Yale has established an excellent precedent in asking physicians to teach others how to become physicians.

THE BOSTON MEDICAL QUARTERLY

THE forthright title of the new and attractive quarterly bulletin of Boston University School of Medicine and Massachusetts Memorial Hospitals is B M Q — *The Boston Medical Quarterly*. The name alone puts it squarely on the map as independent and local and proud of it; which is, after all, somewhat in the tradition of the area from which it derives its nourishment.

Number 1 of Volume I of *The Boston Medical Quarterly* contains four scientific papers by members of the faculty of Boston University School of Medicine and the staff of Massachusetts Memorial Hospitals, an annual report of the Hospitals, a page of editorials, a report of the Division of Obstetrics and Gynecology, clinical notes, a list of staff publications and three pages of abstracts, all well written and well edited.

Of the various infant publications that the *Journal* has welcomed to the literary nursery in recent years, B M Q rates a particularly warm reception.

The sage and grave law makers of the "old colony times" fully understood the difference between pretenders and those who were tolerably skilled in the practice of the mysteries of medicine.

Boston M. & S. J., *July 3, 1850*

MASSACHUSETTS MEDICAL SOCIETY

DEATH

BURNS — Robert F. Burns, M.D., of Fitchburg, died on June 5. He was in his sixty-seventh year.

Dr. Burns received his degree from Baltimore Medical College in 1908. He was chairman of the Fitchburg Board of Health and was a fellow of the American Medical Association.

His widow and a son survive.

MISCELLANY

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

At the annual meeting of the New England Society of Anesthesiologists held on June 13, the following officers were elected for 1950–1951: president, Dr. Bert Hershenson; vice-president, Dr. James Buskirk; and secretary-treasurer, Dr. Francis J. Audin.

The Society is planning eight meetings for next year to be held on the second Tuesday of every month beginning in October, 1950, and ending with May, 1951.

CORRESPONDENCE

DEPRIVATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held June 15, it was voted to suspend the registration of Dr. Raymond G. Ockert, of Mansfield, because of ill health.

GEORGE L. SCHADT, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

NOTICES

SOUTH END MEDICAL CLUB

The summer meeting and outing of the South End Medical Club will be held at Prendergast Preventorium, 1000 Harvard Street, Mattapan, on Tuesday, July 18, at 12 noon. Dr. Eli Friedman, associate professor of pediatrics, Boston University School of Medicine, and camp physician at the Prendergast Preventorium, will speak on the subject "Progress in Tuberculosis." Luncheon will be served.

All physicians are cordially invited to attend.

MEDICOMILITARY SYMPOSIUM FOR OFFICERS OF FOURTH NAVAL DISTRICT

To keep military reserve medical officers of the armed forces posted on the latest developments in the field of medical science, a medicomilitary symposium for officers of the Fourth Naval District will be held at the United States Naval Hospital, Philadelphia, from October 23 to 28. Rear Admiral Clifford A. Swanson, Surgeon General of the Navy, will open the meetings with an address entitled "The Physician as a Naval Officer." Officers attending the symposium will be welcomed by Rear Admiral Roscoe E. Schuirmann, commandant of the Fourth Naval District; Brigadier General Leonard E. Rea, USMC; Captain Clyde W. Brunson, MC, USN, commanding officer of the Philadelphia Naval Hospital; and Captain J. R. Thomas, Fourth Naval District Medical Officer.

Speeches and panel discussions in aviation medicine, national defense in case of disaster or attack, national preparedness, psychiatry, submarine medicine, surgery and orthopedics will be presented. Physicians selected to head the panels include Brigadier General James P. Cooney, chief, Radiology Branch, Division of Military Application, Atomic Energy Commission; Dr. Perrin H. Long, professor of medicine, Johns Hopkins University School of Medicine; Captain John Poppen, MC, USN; Captain George Lyons, MC, USN; Rear Admiral C. J. Brown, MC, USN; Captain C. W. Shilling, MC, USN; Dr. Frank Braceland; Dr. Joseph Hughes; Dr. Edward Strecker; and Dr. Christian J. Lamberton.

Officers are urged to make hotel reservations well in advance, since no Government housing facilities will be available. The final session of the symposium will be held on Saturday morning, October 28, leaving the afternoon free for officers to attend the Penn–Navy football game.

Attendance at the symposium is not restricted to medical officers of the armed forces. All members of the medical profession are cordially invited to attend.

GRANTS FOR RESEARCH IN CARDIOVASCULAR DISEASE

The Research Allocations Committee of the Massachusetts Heart Association will be glad to consider requests from institutions in Greater Boston for grants from the fund that the Greater Boston Chapter will have available for research in cardiovascular diseases during 1950-51.

Applications should be addressed to the Research Allocations Committee, Massachusetts Heart Association, 500 Commonwealth Avenue, Boston 15, Massachusetts, and should include the endorsement of the administrator or dean of the institution under whose auspices the research project is to be conducted.

EXTENSION OF CLOSING DATES FOR APPLICATIONS FOR POSITIONS AS MEDICAL OFFICER

The closing dates for acceptance of applications for examinations for the positions of medical officer (rotating intern, psychiatric resident, surgical resident and general-practice resident) in St. Elizabeth's Hospital, Washington, D.C., have been extended to October 31, 1950, for rotating intern and until further notice for psychiatric resident, surgical resident and general-practice resident. Applications should be filed with the Committee of United States Civil Service Examiners, St. Elizabeth's Hospital, Washington 25, D. C.

Particulars of salaries and qualifications were announced in the June 8 issue of the *Journal*.

(*Notices concluded on page xvii*)

NOTICES (*Concluded from page 34*)

PHYSICAL THERAPISTS FOR CARE OF PATIENTS WITH POLIOMYELITIS

Physicians may obtain information regarding qualified physical therapists available for patients in the convalescent stage of poliomyelitis from the following members of the American Physical Therapy Association: Connecticut, Miss Sarah C. Johnson, Norton Road, Kensington; Maine, Miss Josephine Poor, Mercy Hospital, 144 State Street, Portland; Massachusetts, Miss Ruth Langley, 331 North Main Street, Randolph (telephone, Randolph 6-0416-W; after September 15, weekdays telephone Trowbridge 6-0550), Mrs. Erica Werner, 10 Atwater Street, Worcester, and Miss Louise D'Ercole, 40 Springfield Street, Springfield; New Hampshire, Miss Mary Bullock, R. F. D. No. 4, Concord (telephone, daytime, Concord 800, night, Concord 2599-R); Rhode Island, Miss Gertrude Cogan, 110 Massachusetts Avenue, Providence; and Vermont, Miss Lillian Kron, 342 Pearl Street, Burlington.

SOCIETY MEETINGS AND CONFERENCES

JANUARY 9–DECEMBER 1. Laboratory Courses at Communicable Disease Center, Atlanta, Georgia. Page 950, issue of December 8.

JULY 17–22. International Congress for Scientific Research. Page xvii, issue of September 1.

JULY 18. South End Medical Club. Page 34.

AUGUST 21–26. International Society of Hematology. Page 888, issue of December 1.

AUGUST 28–SEPTEMBER 1. American Congress of Physical Medicine. Page 428, issue of March 16.

AUGUST 31–SEPTEMBER 7. World Federation for Mental Health. Page 306, issue of February 23.

SEPTEMBER 3–9. International Heart Congress. Page 160, issue of January 26.

SEPTEMBER 7–9. All-Austrian Congress of Physicians. Page 994, issue of June 22.

SEPTEMBER 14. Progress in the Management of Hand Injuries. Dr. Henry E. Marble. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

SEPTEMBER 27–29. Mississippi Valley Medical Society. Page 991, issue of December 15.

OCTOBER 12–14. American Association of Blood Banks. Page 428, issue of March 16.

OCTOBER 14–19. American Academy of Pediatrics. Page 962, issue of June 15.

OCTOBER 23–27. American College of Surgeons. Page xi, issue of June 29.

OCTOBER 23–28. Medicomilitary Symposium for Officers of Fourth Naval District. Page 34.

NOVEMBER 1. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

JANUARY 31. American Academy of Orthopaedic Surgery (see Kappa Delta Award for Research in Orthopedic Surgery). Page 736, issue of May 4.

APRIL 9-13. American College of Physicians. Page 962, issue of June 15.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 13

FRIDAY, JULY 14

*9:00 a.m.–12:00 m. Combined Medical and Surgical Staff Rounds. Peter Bent Brigham Hospital.

*10:00 a.m. Surgical Clinic. South End Health Unit, 57 East Concord Street, Boston.

12:00 m.–1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

*1:30 p.m. Tumor Clinic. Out-Patient Department. Mount Auburn Hospital, Cambridge.

MONDAY, JULY 17

*11:30 a.m.–12:15 p.m. Clinical Conference. South End Health Unit, 57 East Concord Street, Boston. Dr. Cleaveland Floyd in charge.

*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.

TUESDAY, JULY 18

*12:00 m. Summer Meeting and Outing of South End Medical Club. Prendergast Preventorium, 1000 Harvard Street, Mattapan.

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

WEDNESDAY, JULY 19

*12:00 m.–1:00 p.m. Grand Rounds. Amphitheater, Children's Hospital.

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